PUBLIC HEALTH REPORTS

In this issue

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CONTENTS

Continued ▶

frontispiece

Ox-drawn sledge carries spraying team in war on mosquito vectors in the Philippines (see paper on pages 687–695).

CONTENTS *continued*

PUBLIC HEALTH REPORTS

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U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
MARION B. FOLSOM, *Secretary*

PUBLIC HEALTH SERVICE
LEROY E. BURNEY, *Surgeon General*

This interim report on prophylaxis of rabies in man reviews briefly the development of experimental studies with laboratory animals and presents results to date of tests of such experimental methods applied to man.

Rabies Prophylaxis in Man

KARL HABEL, M.D.

IN GENERAL, research in rabies prophylaxis has developed along two lines. One has been aimed at improving the effectiveness of rabies prophylaxis in man; the other has been concerned with methods of reducing the severity of reactions to vaccine prophylaxis, especially reactions of the dangerous neurological type.

Efforts to improve the efficacy of prophylaxis were stimulated by the demonstrated failure of vaccine in preventing rabies after severe exposure. Experience in Middle East countries, such as Iran, showed that persons severely bitten by rabid wolves developed rabies at the same high rate (40 percent) whether given a full course of potent vaccine or no treatment (*1*). Research in recent years has centered on the use of rabies antiserum as an adjunct to vaccine. In laboratory experiments with modern quantitative techniques, antiserum alone gave better results against experimental infection than vaccine alone; furthermore, antiserum alone tended to prolong markedly the incubation period. Best protection was obtained when antiserum was used together with a course of vaccine (*2*, *3*).

Dr. Habel is chief of the Section on Basic Studies, National Institute of Allergy and Infectious Diseases, Public Health Service. He presented this paper at the annual meeting of the American Public Health Association, November 1956, Atlantic City, N. J.

In order to determine whether doses of vaccine and antiserum practical for use in man would give similar results, the World Health Organization's Expert Committee on Rabies set up two studies. The first study observed effects on normal human volunteers given various schedules of vaccine either exclusively or combined with a single dose of antiserum. Evaluation of efficacy was based on the serum neutralizing antibody titers developing in the blood of the volunteers at various intervals during and after the course of immunization. A summary of some of the results of this experiment, the details of which have been published by WHO (*4*), is given in figures 1 and 2. Ten persons were observed in each treatment group, and the points on the graph represent the average serum titers of the 10 patients at the specified number of days from the start of treatment.

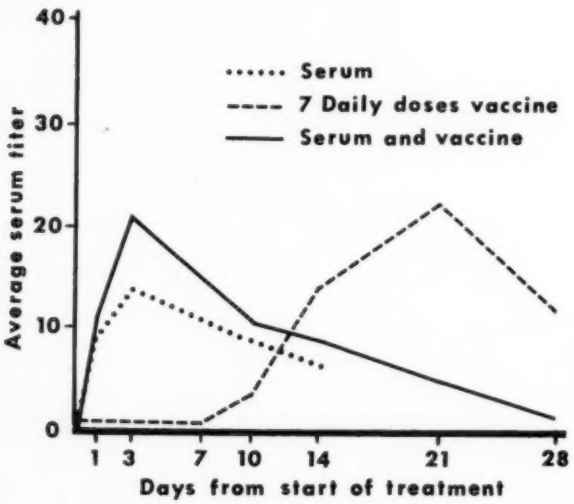
In figure 1 it can be seen that the individuals receiving serum alone in the form of a single injection of antirabies rabbit serum had demonstrable antibody 1 day later; the antibody gradually decreased in titer to the 14th day. The group receiving 7 daily doses of vaccine showed first evidence of antibody response at 10 days, but significant levels did not appear until the 14th day and then persisted. However, if antiserum was given 1 day before the start of vaccine, the pattern of antibody level was similar to that in the group which

received serum alone, and there was no evidence of an active antibody response to the vaccine after the 14th day.

Figure 2 shows comparative results when 12 daily doses of vaccine were given. Again, active antibody production due to vaccine alone was not apparent until the 14th day. It was quantitatively higher than after only 7 doses, and it persisted throughout the 28-day period. Here the combination of that same schedule of vaccine with a single dose of serum gave a significant antibody level early because of the passive immunization with antiserum and late because of active immunization with the vaccine.

These experiments and others indicate that there is some interference with the antigenic effect of relatively low doses of vaccine when serum antibody is given early, but this inhibition can be overcome if more vaccine is given over a longer period of time. On the other hand there was no evidence that the vaccination neutralized the antibody in the passively administered antiserum. Obviously, figure 2 shows the type of response in which we are interested. We would like to have antibody present throughout the course of treatment: antibody introduced early by the antiserum that is given passively; antibody produced late by the active response of the individual to the vaccine.

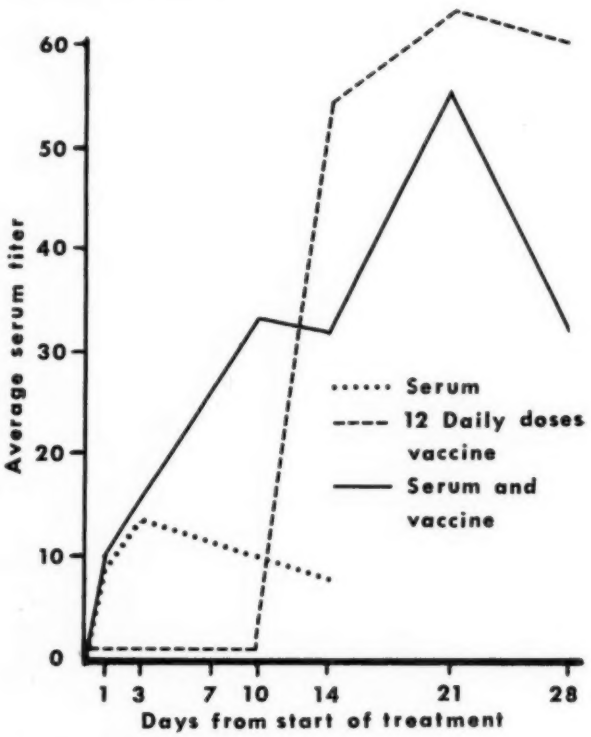
Figure 1. Comparison of neutralizing antibody response of human volunteers to rabies antiserum alone, 7 daily doses of vaccine, and combined treatment.



SOURCE: Reference 4.

NOTE: Each point on the chart represents the average antibody levels of 10 persons and is the reciprocal of the serum dilution which neutralizes 32 LD_{50} of virus.

Figure 2. Comparison of neutralizing antibody response of human volunteers to rabies antiserum alone, 12 daily vaccine doses, and combined treatment.



SOURCE: Reference 4.

NOTE: Each point on the chart represents the average antibody levels of 10 persons and is the reciprocal of the serum dilution which neutralizes 32 LD_{50} of virus.

Field Test in Iran

The second study set up by the WHO Expert Committee on Rabies for the use of antiserum in man was an actual field test in exposed individuals. Because of past experience of vaccine failures in prophylaxis following bites by rabid wolves in Iran, test arrangements were made with Dr. M. Baltazard at the Pasteur Institute in Teheran. Groups of individuals subsequently exposed were to be divided into treatment groups so that comparable exposures could be treated either with vaccine alone or

with vaccine plus antiserum. As frequently happens no such group of exposed individuals became available for some time. When they did more than 3 years later, the local physician was not aware that the bites represented exposure to rabies since the wolf was not apprehended. No treatment was administered until the 20th day when the first of the 17 bitten individuals developed rabies. Although vaccine treatment of the rest of the group was started at this time, the interval between exposure and treatment was so long that the entire group can be considered as receiving no specific prophylaxis. Forty percent of these individuals died of rabies.

One year later an ideal group presented itself, and the story of the exposure is indeed a dramatic one (*5*). In August 1954, several busloads of people stopped to spend the night at a small town in the forests some 500 kilometers from Teheran. Because of the heat many bus passengers and townspeople slept outdoors on the ground or on open porches and balconies. At midnight a scream was heard from an orchard on the edge of town because a large wolf had attacked one of the sleeping men. Within a very short time the wolf bit several others in the orchard, circled a bit and entered the center of the village, where he attacked and bit several people on the street. He even entered some homes slashing people asleep on a balcony and proceeded across town attacking more along the main road. The wolf finally bit six cows in a nearby field and was killed as he lunged at a horse and rider. A total of 29 people, 1 dog, and 6 cows had been bitten during a 5-hour period.

All exposed individuals plus the dead wolf were placed in a commandeered truck and taken to the Pasteur Institute in Teheran, where treatment was started within 30 hours after exposure. The wolf was proved rabid by isolation of rabies virus from his brain. His saliva apparently had been infectious throughout the period of his attack since the first person bitten died of rabies as did two of the cows which were bitten just before the wolf was killed. The patients were divided into treatment groups (table 1). Only the 18 bitten on the head or neck are important in evaluating the treatment results since past experience in Iran had indicated that most rabies deaths occurred after this type of exposure.

A group of 5 patients, 4 of whom had severe bites, were treated with two inoculations of serum given 4 days apart plus a full 21-day course of vaccine; no cases occurred. Another group of 7 patients received one dose of serum on the first day, followed by 21 doses of vaccine; 1 out of the 7 died from rabies. The third group, consisting of 5 individuals, 4 of whom had been severely bitten on the head, received the course of vaccine alone. Of this group, 3 died of rabies. One boy, patient No. 27 listed separately in table 1, was bitten directly through his skull and received practically an intracerebral inoculation of saliva from the rabid wolf. He was unconscious on arrival

Table 1. Mortality of patients bitten by rabid wolf, Iran, 1954

Group	Number of patients	Number of patients with severe exposure	Location of bites	Treatment	Mortality
A	5	4	Head	2 inoculations of serum plus vaccine.	0/5
B and patient No. 28.	7	7	Head	1 inoculation of serum plus vaccine.	1/7
C	5	4	Head	Vaccine only.	3/5
Patient No. 27	1	1	Meninges	6 inoculations of serum plus vaccine.	0/1
D	4	0	Trunk and extremities	1 inoculation of serum plus vaccine.	0/4
E and patient No. 29.	7	0	Trunk and extremities	Vaccine only.	0/7

SOURCE: Reference 5.

Table 2. Neutralizing antibody levels in serum samples of group A patients exposed to head and neck bites of rabid wolf and treated with two doses of serum and complete course of vaccine

Patient No.	Outcome	Antibody titers on days after start of treatment [1]																
		1	3	4	5	6	7	8	10	13	15	19	21	25	29	33	41	53
A1	S	8	+	----	22	----	+	----	22	----	22	----	22	----	5	----	+	12
A2	S	13	+	----	32	----	+	----	22	----	22	----	12	----	6	----	+	3
A3	S	tr	----	----	13	----	+	----	66	----	30	----	76	----	191	----	+	76
A4	S	tr	+	----	----	32	+	----	22	----	22	----	12	----	6	----	----	tr
A5	S	6	+	----	112	----	+	----	10	----	17	----	22	----	22	----	+	8
27 [2]	S	----	----	19	----	38	----	99	112	99	+	30	----	32	----	22	----	----

[1] The figures shown are the reciprocals of the serum dilutions, representing the 50 percent end point in the neutralization test against 8–46 LD_{50} of virus.

[2] Patient 27 received 6 injections of serum and a complete course of vaccine.

S = Survived. D = Died of rabies.
+ = Virus neutralized by undiluted serum; no titration of antibodies done.
tr = Partial neutralization of virus at a dilution of less than 1:5 of serum.

SOURCE: Reference 6.

at the Pasteur Institute. Because of his severe exposure, he was given not only the course of vaccine but also a dose of serum on alternate days for 6 doses. That boy also survived. The other cases listed at the bottom of table 1 are not significant because they were bitten elsewhere than on the head, and we know that even without treatment most of them probably would have survived.

Dr. Hilary Koprowski and I received the serums from all these patients (blood samples were taken at intervals for a period of 50 days by the group in Teheran), and quantitative neutralization tests for rabies antibodies were run on certain of the samples (*6*). Group A, which received 2 doses of serum plus a course of vaccine, showed no antibody, of course, before treatment. Antibody was demonstrated on the first day and persisted at good levels on the 5th and the 10th days. In serum specimens collected at later periods when antibody is not expected to persist, we found that these individuals were developing active antibody as a result of the vaccine. All of these people survived; all of them had antibody (table 2).

In group B, which received only one dose of serum plus a course of vaccine, the one person who died of rabies showed no active antibody response to the vaccine although he had shown antibody levels early after the inoculation of antiserum (table 3).

Of the 5 patients in the control group, which received vaccine only, 3 died of rabies (table 4). There seems to be very little or no correlation between the amount of antibody produced by the active immunization and the subsequent outcome of the disease. One patient who died had no antibody at any time, yet another with fatal outcome had an excellent antibody response. Of course, we have to remember that the antigen of the street virus introduced by the rabid wolf multiplies during the incubation period and can also call forth an antibody response. So it is very difficult in such a study of exposed individuals to evaluate the antibody levels appearing late in the course of immunization. Also in this vaccine group was an individual who survived and yet at no time during the entire course of treatment had any antibody. In my opinion, this individual is one of those persons who do not respond to antigens and I think, undoubtedly, never had an effective exposure to rabies.

As a result of the earlier experimental data and these field trial results, the WHO committee has recommended the routine use of a single dose of antiserum followed by a course of at least 14 doses of vaccine for all severe exposures (*7*). Two further practical points on the use of antiserum should be mentioned. Experimental results as yet untested in the field indicate that local infiltration of part of the total dose of antiserum about the bite wound increases its effectiveness. Finally, the anti-

Table 3. Neutralizing antibody levels in serum samples of group B patients exposed to head and neck bites of rabid wolf and treated with one dose of serum and complete course of vaccine

Patient No.	Outcome	Antibody titers on days after start of treatment [1]												
		1	3	5	7	10	12	15	17	19	21	29	41	53
B1	S	6	+	22	+	6	------	tr	------	------	8	tr	tr	13
B2	D	tr	+	20	+	tr	tr	tr	tr	tr	------	------	------	------
B3	S	6	+	10	+	6	------	5	------	------	5	13	6	------
B4	S	tr	+	8	+	13	------	18	------	------	6	8	+	13
B5	S	0	+	15	------	13	------	tr	------	------	5	tr	------	------
B6	S	tr	tr	6	tr	8	------	8	------	------	30	67	------	112

[1] See footnote 1 and legend, table 2.

SOURCE: Reference 6.

Table 4. Neutralizing antibody levels in serum samples of group C patients exposed to head and neck bites of rabid wolf and treated with complete course of vaccine only

Patient No.	Outcome	Antibody titers on days after start of treatment [1]													
		1	3	5	7	10	15	19	21	25	29	33	41	45	53
C1	D	0	0	0	0	0	0	22	50	85	66	-----	-----	-----	-----
C2	S	0	0	0	0	0	0	tr	5	13	6	-----	19	-----	5
C3	D	0	0	0	0	0	0	-----	0	0	-----	-----	-----	-----	-----
C4	D	0	0	0	0	0	0	tr	-----	18	27	22	15	89	18
C5	S	0	0	0	0	0	0	-----	-----	-----	0	-----	0	-----	0

[1] See footnote 1 and legend, table 2.

SOURCE: Reference 6.

serum presently available commercially in this country is a concentrated horse serum, and tests for sensitivity must be performed before its use. Serum sickness in from 5 to 20 percent of the treated cases is to be expected.

Vaccination Schedules

Research effort in recent years aimed at reducing the severity of prophylactic measures and reactions to them stems from two facts.

First, the currently used rabies vaccine is still a crude biological product. The vaccine is a heavy suspension of rabies infected rabbit brain in which the virus has been inactivated by various chemical or physical agents. Fourteen to twenty-one or more injections are made with this crude brain emulsion in as many days. All treated patients get local reactions, usually of moderate severity. Also, the necessity of a large number of daily visits to the physician requires actual physical residence at a center where treatment is available. This is a hardship for those patients whose homes are far from a medical facility.

The second fact concerns severe and dangerous reactions to the vaccine, the most important of which involve the central nervous system. Experimental work by Morgan (*8*), Rivers and associates (*9*), and others strongly suggests that these reactions are directly related to the multiple injection of the brain tissue contained in rabies vaccine. The relative importance of this postvaccinal problem of encephalitis or paralysis varies in different parts of the world. In general, we in the United States are more concerned than rabiologists in other countries. Other than concern about the influence of poor reporting on the evaluation of the severity and frequency of reactions, the chief reason for American interest probably lies in the fact that, with our low mortality from rabies, it is estimated we have more cases of central nervous system reactions to vaccine than deaths from

the disease. Ten to twenty-five percent of these reactions are fatal.

Because of the severity of the procedure, the practical difficulties involved, and the fact that the occurrence of postvaccinal CNS reactions seem related to the number of injections of brain tissue, investigations are under way to determine the feasibility of reducing the number and size of vaccine injections. Fox and associates (*10*) have shown that 3 doses given 5 days apart give good serum antibody levels in man. This type of study in nonexposed human volunteers is currently being investigated further by the WHO committee. Tables 5 and 6 show the results of our experiments in mice in testing the relative efficacy of different schedules of immunization (*11*). Table 5 shows the effect of variations in number and spacing of vaccine doses when the total dose is the same for all groups, and table 6 evaluates the same effect when each individual dose is the same in all groups. In either case, it is obvious that daily doses did not give much better protection against intracerebral virus challenge or produce antibodies at a significantly higher level than some of the less severe schedules. In general, these results indicate the importance of 2 or 3 early primary doses followed by a booster dose at or after the 10th day.

Table 5. Effect of same total vaccine dose given in various schedules on immunity to intracerebral challenge and neutralizing antibody response in mice [1]

Group	Dose (ml.)	Days	LD_{50} protection (logs)	Serum dilution 50 percent neutralization
A	0.1	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12.	3.7	187
B	.4	1, 5, 10	3.4	56
C	.6	1, 10	2.9	80
D	.2	1, 3, 5, 8, 10, 12.	4.1	68
E	.6	1, 8	2.2	32
F	.4	1, 2, 8	2.2	46
G	.3	1, 2, 3, 8	2.2	56
H	.3	1, 2, 3, 10	3.3	187
K	.4	1, 2, 10	2.6	95
L	.3	1, 2, 8, 12	3.3	279
M	.3	1, 2, 3, 12	3.3	279
O	.4	1, 2, 12	2.6	162

[1] Ultraviolet irradiated vaccine was used diluted to 0.6 percent suspension. Intraperitoneally immunized mice were bled on the 14th day and challenged intracerebrally on the 15th day.

SOURCE: Reference 11.

Table 6. Effect of various vaccine doses and schedules on immunity to intracerebral challenge and neutralizing antibody response in mice [1]

Group	Days	LD_{50} protection (logs)	Serum dilution 50 percent neutralization
A	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12.	4.2	944
B	1, 5, 10	3.3	1,084
C	1, 3, 5, 8, 10, 12	>4.7	>3,125
D	1, 2, 3, 10	3.2	625
E	1, 2, 8, 12	2.1	64
F	1, 2, 3, 12	3.5	71
G	1, 10	1.1	90
H	1, 2, 12	1.4	43
K	1, 2, 10	2.3	215

[1] Phenolized vaccine was used diluted to 1 percent suspension. Intraperitoneally immunized mice were bled on the 14th day and challenged intracerebrally on the 15th day. All individuals were given 0.2 ml. of vaccine.

Avian Embryo Vaccines

Other studies have attacked the problem of reactions to brain tissue vaccines from the standpoint of finding effective vaccines in which the factor responsible for these reactions has been removed or of making vaccines from material other than brain tissue. The former has been accomplished in the laboratory but has not proved practical in vaccine production (*2*). A fair amount of research has been carried out by Fox (*10*), by the WHO rabies committee (*4*), and by Dr. Hilary Koprowski on the possible use in man of live attenuated chick embryo rabies vaccine similar to that currently used in canine immunization. Thus far, this vaccine has been given to several hundred individuals with no deleterious effect. However, in contrast to results in dogs a single dose does not produce immunity in man as indicated by a serum antibody response. Several booster doses are required before antibody becomes demonstrable. In other words, in the dog this vaccine acts as a live virus vaccine with multiplication of the attenuated virus, but in man it acts as an inactivated virus vaccine, and the

virus probably does not multiply. Fox has shown good antibody response after 3 intradermal doses given 5 days apart, and Koprowski has evidence that a single intradermal dose given to individuals who have received rabies vaccine even several years previously will have a booster effect and result in a prompt antibody rise.

In a recently developed vaccine, now commercially available, the rabies virus is produced in duck embryos and is inactivated by beta propriolactone (*12*). This "killed" virus vaccine when used in multiple doses comparable to the brain tissue vaccines is effective in protecting experimental animals against virus challenge and in producing an antibody response in man.

In conclusion, there is hope in the future for the development of a rabies vaccine devoid of the potentiality of producing severe or fatal central nervous system reactions, but by far the most significant recent accomplishment in the field of rabies prophylaxis in man has been the further development of rabies antiserum and the demonstration in a clinical trial of its superior efficacy when combined with vaccine.

Summary

Previous experimental evidence of the greater efficacy of rabies antiserum as an adjunct to rabies vaccine over that of vaccine alone has been confirmed in a dramatic clinical trial. Two doses of antiserum given 4 days apart together with 21 daily doses of vaccine completely protected 5 individuals severely exposed by the bite of a rabid wolf in Iran. One of seven comparably exposed patients who received one dose of antiserum plus a course of vaccine died of rabies, while 3 of 5 receiving vaccine alone succumbed. Serum antibody studies of blood samples of these individuals showed the presence of antibody early and late in the course of treatment in those receiving both serum and vaccine but only in the late period when vaccine alone was used.

Experimental investigations in animals and in man suggest that the number of doses of vaccine may be reduced with proper spacing without markedly reducing its effectiveness. The importance of a booster dose given 10 days after the primary doses was apparent.

Attempts to eliminate severe neurological reactions to rabies vaccine have stimulated research with two types of vaccine produced from avian embryos. In laboratory tests, both appear comparable to the currently used brain tissue vaccine.

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431430—57——2

Taking Care of Diabetes

ELEVEN FILMSTRIPS IN SOUND AND COLOR

Audience: The patient and his family.

Availability: Loan—Communicable Disease Center, Public Health Service, 50 7th Street, NE., Atlanta, Ga. Purchase—United World Films, Inc., 1445 Park Avenue, New York 29, N. Y.

Designed to help the diabetic patient and his family, each of the 11 filmstrips depicts some phase of the problem of diabetes control. These 35-mm. filmstrips, originally produced in 1950, were reissued in 1956.

What Is Diabetes? *47 frames, 8½ minutes.* Helps a patient develop a wholesome attitude toward diabetes by giving him a better understanding of his condition and how it can be controlled; emphasizes the need of cooperation with the doctor, acceptance of the major responsibility for management and control of his diabetes, and maintenance of a positive point of view.

Eating for Good Health. *46 frames, 7 minutes.* Stresses the role of food in controlling diabetes and maintaining good health; aids the diabetic and his family in gaining a better understanding of the patient's condition and the foods he may eat.

Insulin and Its Use. *69 frames, 13 minutes.* Attempts to give the patient an understanding of what insulin is, where it comes from, how it functions in the body, and why some people with diabetes need to take it; shows the different kinds of bottle insulin; and illustrates a method of care and handling of the equipment necessary for the injection of insulin, and demonstrates the technique for injecting insulin.

Planning Good Meals. *52 frames, 9 minutes.* Shows the patient how he can plan a wide variety of meals by using his meal plan and exchange list and explains the function of the various kinds of foods—carbohydrates, proteins, fats, vitamins, and minerals—in maintaining health.

Buying Good Food. *50 frames, 8 minutes.* Explains how certain foods are arranged in groups called exchange lists, illustrates how the lists help patients in buying food in ordinary grocery stores, and shows the variety of foods to be selected and their relative value.

Insulin Reaction. *39 frames, 6 minutes.* Helps the person with diabetes recognize and understand the symptoms of an insulin reaction; shows some of the causes, ways of preventing, and effective means of emergency treatment; and points out the serious effects reactions can have on a patient.

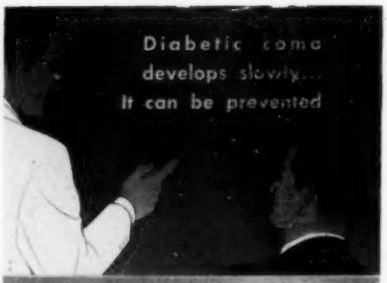
Tests in Diabetes. *38 frames, 6½ minutes.* Shows the relation of urine sugar testing to the degree of control of diabetes, how the patient can test his urine for sugar, and outlines action the patient can take when tests are repeatedly positive.

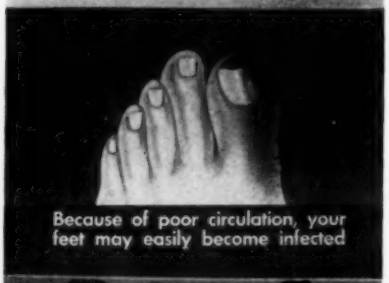
Cooking Good Meals. *40 frames, 8 minutes.* Gives the recommended practices that apply to cooking for the whole family, shows they apply also to the diabetic, and notes different ways of preparing food.

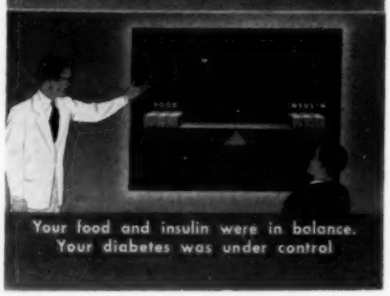
Diabetic Coma. *33 frames, 5 minutes.* Gives some understanding as to what diabetic coma is and how it develops; discusses its seriousness, the need of seeing a doctor when the danger signs appear, and the importance of daily urine and sugar tests, following a meal plan, and taking just the right amount of insulin in order to avoid diabetic coma.

Care of the Feet. *49 frames, 8½ minutes.* Demonstrates why the diabetic patient should take proper care of his feet, how to select proper fitting shoes and socks, and what exercises aid in maintaining good blood circulation and health of the feet; how other serious difficulties from poor circulation, injuries, and infections can be prevented.

Selecting Meals for All Occasions. *52 frames, 8 minutes.* Emphasizes the use of certain basic foods, such as meat, fruit, and milk, for providing variety in food selection and assuring the selection of the right foods to eat in different situations—when one is ill, going on a picnic, eating at a friend's house or at a restaurant, or taking lunch to work.







Radiation Preservation of Food

H. F. KRAYBILL, Ph.D.

SOON after World War II, studies sponsored by the Atomic Energy Commission disclosed that ionizing radiation could be used to preserve foods, and a new concept of food processing appeared. Preservation of food promises to be one of the most important peaceful uses of atomic energy.

Since food spoilage bacteria can be destroyed effectively by radiation with only a small rise in temperature, not more than 10° C., and with remarkable speed, it is conceivable that irradiated foods can be made to surpass in flavor and texture foods preserved by other methods. Current research, sponsored largely by the Department of the Army, is directed toward this goal, as well as the demonstration of safety and nutritional adequacy.

Although many problems regarding the quality of certain irradiated foods remain to be solved, radiation treatment presently offers several interesting possibilities for increasing the supply of perishable food and safeguarding health. At levels much lower than the 2 or 3 million rep (roentgens equivalent physical) necessary for sterilization, radiation inhibits sprouting of potatoes (10,000–30,000 rep), destroys trichina in pork (30,000 rep), increases the keeping quality of perishable foods under refrigeration (50,000–100,000 rep), and destroys insect infestation (50,000–100,000 rep).

Either gamma or electron sources are used for radiation preservation of food. Mixed fission products (spent fuel rods from nuclear reactors) and cobalt-60 are the sources of gamma rays. Resonant transformers, Van de Graaff generators, and linear accelerators are the electron sources. Penetration of radiation from a gamma source is greater than that from an electron source, but a gamma source has the disadvantage of requiring continuous shielding. An electron source can be turned off and on.

Since pasteurization or sterilization of food requires rather high levels of radiation, higher than the level required for lethal effects against mammals and insects but lower than that for viruses and enzymes (fig. 1), it might be anticipated that rupture of chemical bonds would occur during processing. This has been found to be true. The molecular alteration in fat, protein, and carbohydrate in food produces certain noticeable changes in odor, color, flavor, and texture (*1*). The effect of radiation on meat, which has been studied extensively, may be summarized as follows:

- Protein change: Increase in creatinine.
- Production of sulfur compounds: Hydrogen sulfide and mercaptans produced at 70,000 rep.
- Pigmental changes: Oxymyoglobin and metmyoglobin formed.
- Enzyme inactivation: Proteinases inactivated at 1.6×10^6 rep.

Much of the current research work is concentrated on improvement of texture and flavor in an effort to increase acceptability of irradiated food. Foods sensitive to radiation undergo changes in sulfur-containing compounds, proteins, and unsaturated fatty acids as a result of interactions with free radicals during irradiation. One method of counteracting these effects would be the introduction of com-

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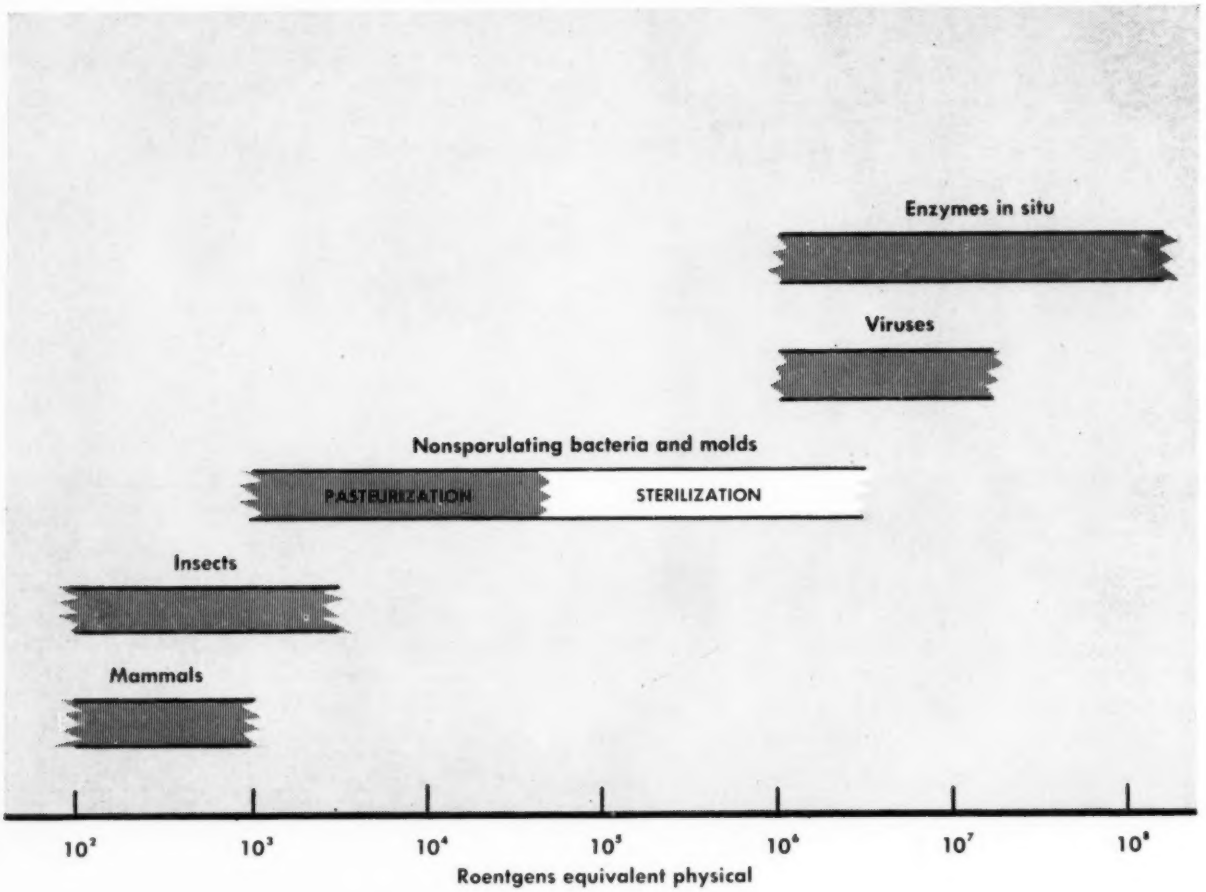
Figure 1. Radiation dosages producing lethal effects in certain biological systems.



pounds that would serve as free radical acceptors. Such compounds, of course, must be acceptable as chemical additives. Other possibilities include packing the food under an inert gas atmosphere (nitrogen or helium, for example), prestoring the food to reduce the available oxygen, blanching prior to irradiation, and vacuum packing.

Since alteration in chemical structure is induced by radiation, it is possible that toxic degradation products may be produced through transformation of the macronutrients (fat, carbohydrate, and protein) and the micronutrients (vitamins) in the foodstuff. Assuming that radiation processing is technologically successful and economically feasible, it is likely that some day a significant proportion of man's diet will consist of irradiated food. It must be demonstrated, therefore, that foods treated with radiation are nontoxic to humans and that they are at least equal in nutritive value to foods preserved by canning or dehydration.

An excellent procedure for evaluating the wholesomeness of radiation-sterilized food has been described by Lehman and Laug (*2*). They suggest that studies on wholesomeness be directed along two major lines: potential toxicity and nutritional adequacy. Absence of induced radioactivity, carcinogenicity, and antigenicity must be established through extensive toxicity testing. Chemical and physical examination of the food prior to animal studies may provide important information for design of the toxicological study. For disclosing toxic effects, it is standard practice to challenge an animal with a relative excess of the test substance. For determining nutritional adequacy, the challenge should be made by reducing the vitamin supplement added to the basal ration to a level at which nutrient inadequacy would be intensified.

Since the various species of animals, and even strains of the same species, frequently differ in sensitivity, a number of different species, such as the rat, the mouse, the dog, the monkey, and the chicken, should be included in the testing program. As radiation-induced changes in food are extremely subtle, the usual gross observations of growth, reproduction, and food consumption may not adequately describe toxic or harmful effects. It is desirable to include in the experiments a measure of cellular metabolism as a supplement to the gross observations. This can best be accomplished through application of enzyme analyses of tissues of the animals on the experimental diets.

Since March 1954 the Office of the Surgeon General, Department of the Army, has sponsored, through contracts with various institutions, a broad research program relating to wholesomeness of irradiated food, as outlined (see inset). Working closely with the Office of the Surgeon General in directing this program is the Food and Drug Administration, Department of Health, Education, and Welfare.

Induced Radioactivity

In first considering the possibilities of preserving food by means of radiation, it was assumed that the process would not induce radioactivity in the food, since gamma and electron sources are used and a neutron flux is not involved. One of the few direct studies of this question supports this assumption: No detectable amount of radioactivity was found in 24 common food elements that had been irradiated with a 1,000-curie cobalt-60 source (*3*).

Investigators are currently considering the possibility that accelerated electrons with beam energies greater than 10 Mev. might induce measurable amounts of radioactivity. Radiation preservation, however, is accomplished with beam energies far below this level. Also, Peterson and associates (*4*) noted that, following a nuclear explosion, food in unbroken containers at a distance of 1,700 feet from ground zero would be safe to eat. Induced radioactivity apparently is no problem in radiation processing of foods, provided no source of neutrons is present.

Toxicity Studies

One of the earliest studies of toxicity was reported by DaCosta and Levenson (*5*). These investigators found that a capacitronized synthetic ration fed to male and female weanling rats produced no deleterious effects on growth. However, there was impairment in the fertility of the male and increased mortality in litters that they believed was due to destruction of vitamin E. These findings were later corroborated by Poling and associates at the Swift and Company Research Laboratories in studies of irradiated ground beef (*6*). They found that male infertility and viability of the young were readily corrected by supplementation of the diet with vitamin E.

Similar studies on irradiated butterfat (*7*) and on irradiated dried whole eggs (unpublished report by B. E. Proctor and John T. R. Nickerson of the Massachusetts Institute of Technology) indicate that these products have a slight effect on growth rate but essentially no toxic effects.

A three-generation mouse-feeding study, in which a semisynthetic diet sterilized by steam

Army Wholesomeness Studies

Short-term feeding (8 weeks). Army Medical Nutrition Laboratory and the University of Colorado: rat and man; Wisconsin Alumni Research Foundation: rat.

Longevity, reproduction, and lactation. Agricultural and Mechanical College of Texas: rat and chicken; University of Michigan: rat and chicken; Oregon State College: rat; Cornell University: dog; Columbia University: rat; Johns Hopkins University: rat; University of Illinois: rat and dog.

Nutritional adequacy. University of Illinois (protein): rat; University of California at Los Angeles (fat): rat; Alabama Polytechnic Institute (vitamins): rat.

Digestibility. University of Rochester: dog.

Carcinogenicity. Wisconsin Alumni Research Foundation: rat and mouse.

Antigenicity of irradiated proteins. Army Medical Nutrition Laboratory and the University of Colorado: guinea pig.

or cathode rays was compared with an unprocessed ration, revealed no differences in growth, general appearance, or reproduction. However, the mice raised on the irradiated diet exhibited some impairment in lactational performance (*8*).

Short-term rat-feeding experiments with irradiated foods have been conducted by the Wisconsin Alumni Research Foundation, the Armour Research Foundation, and the Army Medical Nutrition Laboratory jointly with the University of Colorado to determine whether the foods are potentially toxic and to provide wholesomeness clearance for palatability testing by human subjects at the Quartermaster Food and Container Institute for the Armed Forces. Approximately 40 foods have received clearance by this procedure, and an additional 59 have been approved by extrapolation.

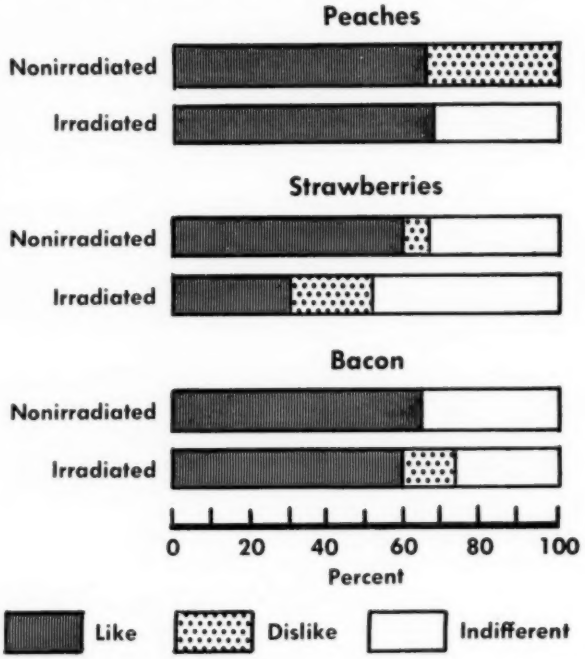
The irradiated foods that have received wholesomeness clearance have been fed for 30 days at levels of 35, 65, 80, and 100 percent of the total calories in the diet to 10 human volunteers at the Army Medical Nutrition Laboratory. No untoward effects have been observed, and the volunteers have indicated equal acceptance of nonirradiated and irradiated foods (treated at 3 million rep) with only a few exceptions (fig. 2).

To evaluate the effects of a diet composed entirely of irradiated food, experiments in which rats receive such a diet are being conducted at the Army Medical Nutrition Laboratory. The diet is so composited as to provide proper levels of fat, carbohydrate, and protein. No adverse effects have developed through the first two generations.

Other longevity experiments with organ meats, pork, and a laboratory basal ration indicate that these irradiated foods are satisfactory for growth when fed at high levels to successive generations of rats. With other test species, such as the dog and the chicken, it has been demonstrated that, in comparison with a nonirradiated ration, irradiated rations support good growth, normal reproduction, and average food consumption.

Because of the possibility that irradiation may produce carcinogens in food, extensive investigations have been conducted by Teply and

Figure 2. Acceptability of typical irradiated and nonirradiated food: percentage distribution of ratings by test subjects.



Kline (*9*) to determine whether irradiated sterols in extracts of egg, yeast, and pork will induce spontaneous tumor formation in rats and mice when injected, fed, or painted on the skin of the test animal. From their experiments to date, there is no clear evidence of the production of carcinogens by irradiation of the food materials under study.

Nutritional Adequacy

The nutritive quality of irradiated food is evaluated by measuring the biochemical effects of ionizing radiation on individual macronutrients and micronutrients, as well as by observation of effects on animals in feeding experiments. Irradiated foods are compared with unprocessed foods and with heat-sterilized foods.

Andrews and co-workers (*10*) have shown that fats having peroxide values of 100 or less are not harmful to rats, whereas higher levels of peroxides produced by irradiation or oxidation are toxic. However, foods sterilized at 3 million rep have peroxide numbers well below 100, usually in the range of 70 to 80.

The effect of gamma radiation on carbohydrate has been studied extensively by Johnson and Metta (*11*). They found no significant alteration in the physiological energy of carbohydrate.

An important criterion in the evaluation of protein quality is the biological value of protein. Johnson and Metta have determined the biological value of the proteins of beef, milk, peas, and lima beans irradiated at 3 million rep, as shown in the table (*11*). According to this study, radiation has virtually no effect on the biological value of beef protein. The biological value of milk protein is reduced about 16 percent by radiation, as compared with about 6 percent by heat. Experiments in which irradiated milk was supplemented with various amino acids indicate that radiation causes a loss of cystine in milk protein. The decreased biological value of irradiated pea protein is probably due to destruction of sulfur amino acids, whereas the biological value of lima bean protein, which was improved considerably by heat but only slightly by radiation, can be accounted for by the destructive effect of heat on trypsin inhibitor.

Effects of heat sterilization and radiation sterilization on biological value of meat, milk, lima beans, and pea proteins

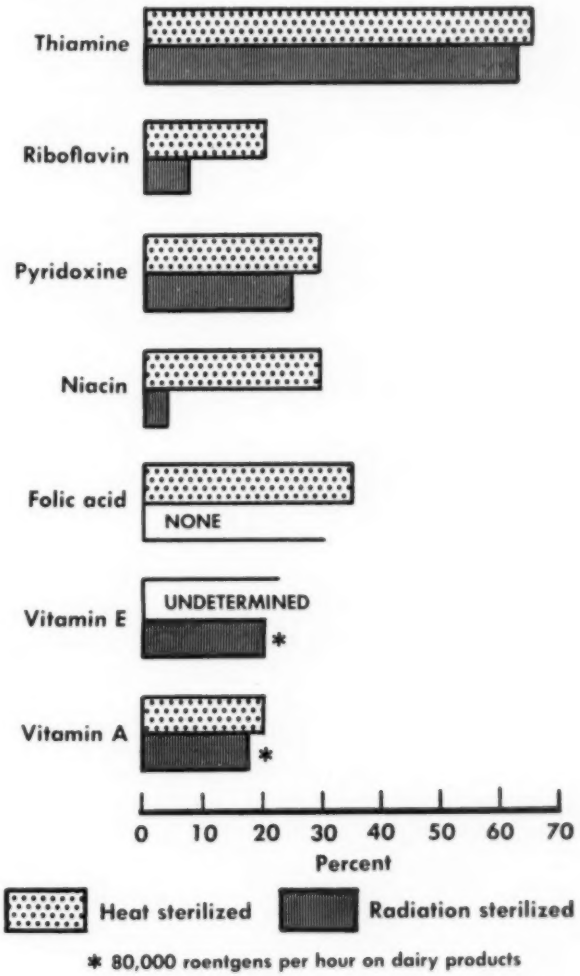
Food	Biological value (percent) [1]		
	Raw	Heat sterilized	Radiation sterilized
Meat	78		79
Milk	90	84	74
Peas	59	58	50
Lima beans	50	68	51

[1] Biological value $= \frac{\text{nitrogen utilized}}{\text{nitrogen absorbed}} \times 100$.

SOURCE: Reference 11.

The fat soluble and water soluble vitamins are sensitive to ionizing radiations, some more so than others. Proctor and Goldblith (*12*) have made extensive studies on the effect of ionizing radiations on the B vitamins. While ascorbic acid is radiosensitive, riboflavin and niacin are radioresistant in dilute solution. Niacin in solution has a protective effect on

Figure 3. Percentage destruction of vitamins in various foods sterilized by heat and by ionizing radiation.



ascorbic acid. Foods act as natural protectors; for example, vitamin B_{12} in milk is decreased only 30 percent, whereas in aqueous solution 68 percent is destroyed. Although the destruction of vitamins due to radiation preservation may appear significant, most investigators feel that the vitamin loss is no greater than that experienced during thermal processing (fig. 3).

Gross effects from feeding irradiated foods to experimental animals have been measured by such indexes as growth, reproduction, and lactational performance. More recently, however, measurements of the activity of representative tissue enzymes involved in the metabolism of potential irradiation end products by the ani-

mal provides more accurate information on the effect of feeding either irradiated or nonirradiated diets. At the Army Medical Nutrition Laboratory we have noted, for example, a higher activity of cytochrome oxidase in tissues from rats on irradiated diets than those maintained on nonirradiated diets. The difference was statistically significant at the 5 percent level. This would suggest that some interruption in lipid metabolism has been effected.

Summary

Treatment of foods with ionizing radiation promises revolutionary advances in food-preservation possibilities. There are still major technological problems in regard to acceptability of certain foods processed with a radiation dose of 2 or 3 million rep. However, treatment at lower radiation levels, which produces such results as inhibition of sprouting of potatoes, destruction of trichina in pork, increase in the keeping quality of food under refrigeration, and destruction of insect infestation, is generally successful.

In experimental work undertaken thus far, radiation-sterilized foods have not been found toxic, nor has any evidence of carcinogenicity appeared. In animal feeding experiments with a wide variety of irradiated foods, reproduction and lactational performance in general are the same as for animals maintained on nonirradiated diets. One worker, using an irradiated synthetic diet, demonstrated slight impairment in lactational performance of mice, but this effect has not been induced in other animal species by feeding them irradiated foods. The nutritive value of these foods has been found to be equivalent to that for heat-processed foods.

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OTIS L. ANDERSON, M.D.

Training Opportunities FOR PUBLIC HEALTH PERSONNEL

From a 10-State survey it has been estimated that some 17,000 professional positions in State and local health departments throughout the country call for graduate or specialized public health preparation, and that almost 9,000 persons in these positions have not had such training. Thus, more than half of our Nation's public health workers have not had the training that provides a sound and balanced knowledge of the multidisciplinary technical aspects of health problems and of the relationship of health problems to the socioeconomic fabric of the community.

DURING the past decade new research discoveries and developments in the health sciences have immeasurably enhanced the potential benefits of public health protection. Many health authorities have been quick to accept and to plan for the broader concepts in public health which have evolved from these developments. But they have been faced within the same period with an acute and worsening shortage of trained health personnel in all categories. In many States and communities, as well as in Federal agencies, plans and hopes remain unfulfilled because the kind and number of personnel needed to translate ideas into action have simply not been available. The problem has been with us for a long time, but it has become more pointed with each forward step in public health techniques and practices.

The need for more and better qualified personnel has been further intensified by the growth in the population to be served by public health programs. Since 1951 there has been a 10 percent increase in our national population. During these same years, the number of full-time personnel in State and local health departments has increased only 6 percent.

Indeed, we actually have fewer physicians and engineers in public health today than we had in 1951, with 15 million more persons to be served. According to recognized standards, we have less than half the physicians and nurses needed to extend basic minimum health services to the entire country—and not quite two-thirds the number of sanitation personnel that would be required. Besides this basic personnel, the newer health programs require a

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steadily increasing corps of workers representing a wide variety of professional categories. In addition, there are many demands for health personnel for foreign assignments, the armed forces, industry, research, and other official and nonofficial organizations.

Obviously, under these conditions our public health services cannot keep pace. Personnel shortages delay the initiation of needed studies and services concerned with chronic illness and aging, air and water pollution, radiological health, accident prevention, rehabilitation, and other issues brought into focus by our changing economy and population mobility. Further, the shortages hinder the improvement of current programs and prevent the strengthening of local health organization.

The lag is the more unfortunate because of the challenge presented by the forces of today. We see evidence of national vitality in the changing social and socioeconomic structure of the Nation; in the continuing population growth; in the longer life span achieved; in new and expanding industries and job opportunities; in the growth of urban and suburban areas, with ensuing metropolitan complexes. Much of this vitality can be ascribed to the success of the older, traditional public health function of controlling the common communicable diseases—the great killers of their day and dominant obstacles to the social and economic development of this and other countries. Now, in turn, the modern forces are reshaping public health philosophy and practice. The many advances in preventive and curative medicine have also contributed mightily to this reshaping. All these factors have added to the potentials as well as to the complexity of health protection, so that postgraduate training and residencies in public health practice have become as essential to this medical specialty as to the clinical specialties. In point of view, public health has advanced with the times, but its supply of trained workers has not.

Special Training Required

To say that there is a steadily growing need for more public health workers is not enough. Modern public health programs require well-trained personnel. An effective public health worker must have, in addition to sound competence in his profession (medicine, nursing, engineering), an understanding of how to apply his basic discipline to community health problems. He must know how to take full advantage of available resources, how to make maximum use of recently developed scientific knowledge in the prevention and control of disease.

Each member of a health department staff must be keenly aware of the importance of good relationships among the several professions which make up the public health team. He must fit his own skills and knowledge smoothly into a complex organization.

Even the most dedicated and basically well-prepared employee learns these things more readily by special training than solely by instinct and on-the-job experience. Training alone does not make a superior health worker. Nevertheless, in general, the competence of the individual who already possesses other qualities essential to success in his field will be increased with advanced public health training.

One of the most critical areas of need is for trained public health physicians. The total number of physicians employed by State and local health departments has actually decreased since 1950. Last year, in health officer positions alone there were 436 vacancies. The application of specialist techniques in public health, requiring a wide variety of professional and ancillary personnel, makes all the more necessary the well-trained medical generalist who can see the public health program as a whole and maintain a balance in its direction. To fill these administrative positions adequately, physicians need formal public health training.

Such training is also highly important for other professional members of the modern public health team. A nurse's basic training is focused on bedside care of the sick. In public health, her primary purpose is preventing disease and disability. In order to do this effectively, she must learn to redirect her fundamental knowledge. The sanitary engineer, too, must learn the public health application of his skills in meeting community sanitation problems and in controlling environmental health hazards.

In addition to physicians, nurses, and sanitary engineers well-grounded in public health, present-day programs require the services of dentists and dental hygienists, health educators and nutritionists, laboratory technicians and veterinarians, statisticians and medical social workers, and a growing array of other groups with professional training supplemented by orientation to the public health aspects of their special fields.

Despite the seriousness of the situation with regard to trained personnel, efforts to improve it dwindled over a number of years. From a high point in 1947, when more than 900 persons in State and local health departments were given more than 4 months' training during the year, the annual number steadily declined to a low of 373 in 1956. Further, during that year 35 States had no physicians in training; 34 States had no engineers or sanitarians in training; and 17 States had no nurses in training—although shortages were, and are, most severe in those categories.

In recent years short-term nonaccredited courses sponsored by State and local health departments have, in large measure, replaced accredited postgraduate training in public health. For example, a number of States have established field training programs, designed to meet immediate needs of personnel in specific professional and subprofessional groups. These courses offer much of value, particularly in sanitation, laboratory, and related areas. A considerable amount of necessary training and vocational experience can also be supplied through orientation classes, inservice training, refresher courses, institutes, and workshops dealing with general areas of public health and with particular health problems. However, this brief, informal instruction, though important, is in no way a substitute for postgraduate education. It does not replace the broad indoctrination in public health provided by academic courses of study.

Training Funds

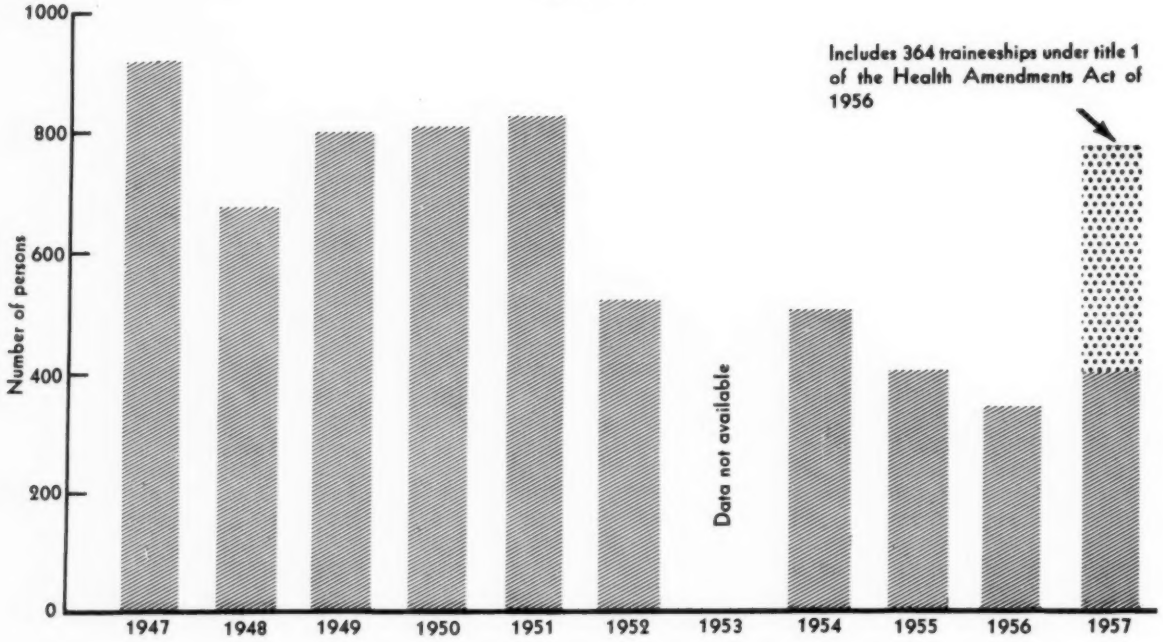
The financing of training, particularly accredited professional training, must, of course, compete in health department budgeting with the financing of the whole range of health programs and services for which, it is safe to say, no health department has completely adequate resources. In planning the expenditure of available funds, however, setting aside a portion to provide formal public health training for staff members, present and future, is wise budgeting, even if it means resisting for the moment pressure for desirable current activities. Funds expended for training are an investment in the future.

There is evidence that many State health departments are fully aware of the wisdom of such an investment, that they are willing to assume their part of the joint Federal-State responsibility for improving the competence of personnel—when funds can be so used without sacrificing basic operations. However, since 1950, Public Health Service grants to States for preventive health services have shown a downward trend, from almost $45,000,000 in 1950 to not quite $22,500,000 in 1956. Because about 75 percent of their training activities had been supported over the years by Federal grant funds, State and local health departments were too hard pressed in many instances to consider more than minimal training courses for their employees.

Then for fiscal year 1957 the health grant total increased about 30 percent over 1956, to slightly more than $29,000,000. Along with this brighter financial picture, fiscal year 1957 also shows, for the first time since 1951, a reversal of the downward trend in number of persons receiving advanced training under State and local sponsorship (see chart). The gain between 1956 and 1957 amounts to 8 percent (401 persons as against 373) and is reflected among 9 of the 15 occupational categories represented.

There are other hopeful signs, such as the increased enrollment in schools of public health—from 570 graduate or special students in the academic year 1949–50 to 874 during 1956–57 (excluding foreign students). Also more States and Territories are providing training opportunities. In 1957 there were 47 States sponsoring public health training as against 40 States in 1954; and in 1957, 75 percent of the trainees were sponsored by 16 States,

Number of persons receiving full-time accredited sponsored training of 4 months or more, fiscal years 1947–57.



as against only 8 States as chief sponsors in 1954.

These indications of progress are indeed welcome. But at this stage of cumulative needs and shortages, it is clear that some assistance over and above increased health grant funds is necessary if we are to avoid a serious lag in meeting total public health needs for a growing population and economy. New people must be drawn into the field not only to augment current staffs and programs, but also to provide a reserve from which replacements can be drawn. For example, an estimate, based on the 10-State sample survey, indicates that some 450 trained professional employees were lost to health departments in 1956 for such reasons as resignation, death, and transfer to jobs outside of official health agencies. In 1955 the loss was 546 workers. Thus, the group of 401 State-sponsored trainees in 1957 will not provide sufficient replacements for even normal attrition in health departments.

New Forces Toward Solution

Leaders in the field saw the situation as increasingly wasteful of valuable knowledge, gained in large part through the basic research activities long and strongly supported by the Federal Government. Potentially effective public health planning, based on the newer developments in the health sciences, lay dormant instead of being applied to the never-ending fight against disease, disability, and death. Within Congress there was serious concern and desire for immediate action, plus recognition of the fact that understaffed health departments and agencies needed assistance in meeting the problem.

The Health Amendments Act of 1956 became law (P. L. 911, 84th Cong.) on August 2, 1956. Under title I of this act, Congress authorized the Public Health Service to establish a program to provide graduate or specialized public health training for health personnel in a variety of professional fields, and appropriated $1 million for the first year's operation.

The bill was also specifically concerned with stimulating advanced training for professional nurses (title II) and with expanding and improving vocational training programs for practical nurses (title III). Each of these two programs received $2 million for fiscal year 1957.

We are concerned here with title I of the Health Amendments Act. The basic purpose of this section is to alleviate the serious lack of

trained personnel in State and local health departments through a traineeship program which will bring into the field new people adequately prepared in all the needed disciplines. It is designed to supplement, and not to replace, the training activities currently sponsored by State and local governments. This aim promises a measure of relief to the health director long harassed by vacant positions and with consequent doubling-up of duties and responsibilities to the point where the release of even one staff member for full-time academic training makes worse an already bad situation. He is in the position of having to postpone the very measures that would improve staff efficiency and thereby relieve the burdens of understaffing.

In order to encourage new people to enter upon careers in the field of public health, this program seeks trainees among qualified individuals with less than 2 years' experience in public health work and less than 1 year of graduate or specialized public health training. Moreover, special attention is given to age (by a preference for candidates under 35), to the candidate's plan for using the training, and to his plans for future employment. Certain other aspects are also given consideration, such as geographic distribution of candidates and the degree of shortages in the professional categories.

The traineeships are generally to be awarded for a period not to exceed 12 months. They are open to physicians, nurses, sanitary engineers, sanitarians, health educators, laboratory personnel, veterinarians, dentists, statisticians, nonmedical administrators, and other professional personnel whose skills are required in modern public health practice. In short, opportunities are offered to men and women who have completed their basic professional education to receive postgraduate training in public health. The traineeship awards are offered to them either directly by the Public Health Service or through grants to schools of public health and to colleges and universities offering public health nursing.

At the end of this program's first fiscal year of operation, 364 persons had been awarded traineeships for public health training to begin during the 1956–57 academic year, and the entire fiscal appropriation of $1 million had been used.

Remarkable success has been achieved in a short time toward fulfilling the objectives of the traineeship program as to age and status of

Number of individuals awarded public health traineeships under title I of the Health Amendments Act of 1956 according to professional category, as of June 30, 1957

Professional category	Number of trainees	Age			Years of previous public health training		Years of previous public health experience			
		Under 35	35–45	Over 45	Less than one	One or more	0	0–2	Over 2 through 5	Over 5
Physicians	21	13	7	1	21	0	10	4	7	0
Nurses	199	161	36	2	199	0	101	66	21	11
Sanitary engineers	27	25	2	0	25	2	12	6	3	6
Sanitarians	25	20	5	0	24	1	3	5	12	5
Laboratory personnel (bacteriology, immunology, chemistry, etc.)	13	13	0	0	10	3	4	6	2	1
Statisticians	2	2	0	0	2	0	0	0	1	1
Health educators	36	23	13	0	35	1	20	6	7	3
Nutritionists	6	6	0	0	6	0	5	1	0	0
Medical social workers	1	0	1	0	1	0	0	0	1	0
Dentists	10	4	6	0	10	0	4	4	1	1
Dental hygienists	8	6	2	0	8	0	4	1	3	0
Veterinarians	9	5	4	0	9	0	4	1	3	1
Nonmedical administrators	7	5	2	0	7	0	5	1	1	0
Total	364	283	78	3	357	7	172	101	62	29

trainees, and distribution among professional categories and among suitable academic institutions (see table). Of the 364 individuals given traineeships through June 1957, more than three-fourths were under the age of 35. Most of the remainder were between 35 and 45 years. Only three persons were over the age of 45.

Somewhat fewer than half of the total receiving traineeships, 172 persons, had had no previous experience in the field of public health. Of the remaining 192 trainees, 101 had had 2 years' or less experience in public health; 62 had been in such work for from more than 2 years through 5 years; and only 29 had been in the field for more than 5 years.

Awards were made to representatives in 13 different professional categories. The academic institutions where the trainees studied included 11 schools of public health; 32 colleges and universities offering public health nursing (with recognized programs allowing a major in public health nursing); and 19 other institutions, including 14 engineering schools.

In December 1956 a national advisory committee appointed by the Surgeon General to assist the Service in planning the 1957–58 operation of the traineeship program met in Washington and reviewed the standards and methods used for the previous year. The committee discussed the merits of broadening the traineeship range in the future to include teachers and research personnel, and of supporting 1 individual for 2 years of training. It also made plans for a national evaluation conference in 1958, which Congress directed as part of the legislation.

In summary, the new program of Public Health Service traineeships in its first year of operation added 364 trainees to the 401 receiving full-time accredited State-sponsored training—a combined total of 765 trained public health workers for potential employment in health departments and agencies. This total group provides a definite upswing to the prolonged decline in such activities. This is a good beginning, even though we realize that training must be provided for an even larger number of current and potential health department employees in the coming years, if we are to enlarge health and personnel resources adequately.

In accordance with the President's request, Congress doubled the appropriation for the traineeship program for fiscal year 1958, providing $2 million for the coming year. With this support, we can expect to see soon some concrete results in terms of increased availability of trained personnel for State and local health departments. It is expected that in the second year of operation, public health traineeship grants will be made to 11 schools of public health and approximately 44 universities and colleges nationally recognized as preparing registered nurses for beginning positions in public health nursing.

On the basis of the 1956–57 accomplishments, this program can be viewed as a definite impetus to the solution of the large and continuing problem of keeping personnel skills at a high level by constant training.

The Rural Health Unit in the Philippines

MALCOLM J. FORD, M.D., M.P.H., and AMADEO H. CRUZ, M.D., C.P.H.

IN the countries of the East, more and more interest is being focused on rural areas because of the rise in population, the importance of food production, and the progress of land tenure reform movements. Providing local health services to rural inhabitants is of major significance and, in the Philippines, the government's health program has recently been recharted to bring these services to every municipality in the Republic.

Historical Review

Public health in the Philippines appears to have been fostered by the Franciscan friars. In 1577, Friar Clemente of the Order of Friars Unilova set up a medical dispensary for the indigent of Manila in the Posteria of the Franciscan convent in the Intramuros, or old walled city of Manila. This eventually became the San Juan de Dios Hospital, which operated at its original site for 368 years, up to the Second World War. Following the creation of this institution, other hospitals were built in many other parts of the Philippines.

In 1690, during the Spanish occupation, the Dominican Padre Juan de Pergero was instrumental in installing a water system for the town of San Juan del Monte and for Manila. Charles IV of Spain sent his personal physician, Dr. Francisco Javier de Balmis, to Mexico, Central and South America, and the Philippines, where he arrived in 1805 to introduce smallpox vaccination. The following year, the Central Board of Vaccination was established. It was the earliest official public health organization in the Philippines. In 1876, the Spanish Government appointed *medicos titulares*, who were essentially the provincial health officers of that day, and, by the end of the Spanish regime, there was an official of this type in every province but one. Most *medicos titulares* were Spanish.

A further step in the development of public health was the creation of the Superior Board of Health and Charity in 1888, and one of the last achievements in health under the Spanish occupation was the addition of a 2-year course in some fundamental medical and dental subjects to the curriculum of the University of Santo Tomas in 1898. Graduates of this course, *cirujanos ministrantes*, served as male nurses and sanitary inspectors. In remote areas, they ministered to the sick in the absence of a physician or dentist.

With the American occupation came a change in health administration. Act 157 of the Philippine Commission in 1901 set up a Board of Health of the Philippine Islands; and in the same year, Acts 307 through 309 provided for provincial and municipal boards of health, with both Filipino and American members.

In 1906, the provincial boards of health were replaced by district health officers with jurisdiction over health districts. The districts were usually coextensive with a province but sometimes encompassed more than one province or parts of provinces. Further evolution in public health took place in 1912 with the "Fajardo Act," which created sanitary divisions, essentially geographic divisions of municipalities within the provinces. They included 1 to 4 municipalities; each was assigned a "president," who had to be a duly qualified

At the time of this study, Dr. Ford was rural health adviser to the United States Operations Mission to the Philippines. He is now chief, Special Health Services, Region 7, Public Health Service. Dr. Cruz serves as project director of the rural health units project, Department of Health of the Philippines.

physician, for supervision of health work. Usually a sanitary inspector and occasionally a nurse were also assigned to the sanitary division.

Dr. Jose Fabella, the first Secretary of Health and Welfare of the Philippines, brought about the establishment of puericulture centers in 1925 for maternal and child health care in local areas. They were supported by voluntary contributions matched by national funds received from the National Sweepstakes Fund. These puericulture centers were staffed for the most part by a nurse or midwife and a woman attendant, assisted by a part-time physician. The program was largely confined to prenatal services concentrating on the delivery event. These centers still suffer from insufficient local support and lack of year-round personnel.

Under Dr. Fabella, municipal maternity and charity clinics were also set up in 1939. They operated in municipalities and municipal districts of less than 8,000 in population and were directed by either a physician, nurse, or midwife. Salaries included a basic compensation and an additional amount for deliveries personally attended, up to a specified maximum. Compensation of personnel assigned to certain hardship areas was doubled if they were nonresidents of these areas at the time of appointment. In some instances, treatment of the indigent sick in these clinics duplicated the work of the sanitary divisions.

In 1947, the Philippine Department of Health reorganized into bureaus: the bureau of hospitals; the bureau of quarantine; and the bureau of health, for supervising preventive health services throughout the country. This reorganization placed administration of city health departments at the bureau level and placed many specialty programs, such as tuberculosis control, health education, and nutrition in the division of laboratories. The municipal maternity and charity clinics were now under the bureau of hospitals, and the sanitary divisions, under the bureau of health.

At the mid-century mark, many separate local health programs had accumulated. The president of the sanitary division was charged with duties in preventive medicine in addition to medical care. Frequently, he had no more than 1 or 2 sanitary inspectors to assist him. He was required by the act creating his office to "provide himself with the necessary appliances and also the instruments for all emergency cases, medical, surgical, and obstetrical." He had an advisory relation only to the puericulture centers. There were about 400 sanitary divisions serving about 1,200 municipalities.

The activities of all local health units were confined almost entirely to the *poblacion* or town center, leaving the outlying *barrios* or rural areas relatively unserved.

The specialty programs concentrated on isolated phases of the health problem, such as malaria, tuberculosis, venereal disease, and health education. A program of immunization, principally for smallpox, was carried out by vaccinating parties, which were made up of nonprofessional workers who covered specified areas. Their schedule called for a visit to each province once in 5 years. Nominally supervising this group of activities in the province was the district health officer, whose actual authority apparently extended only to the presidents of the sanitary divisions. He also had general supervision of the health of the people of the province. The number of sanitary inspectors, nurses, and clerks he had to assist him depended on the size and popula-

ICA photograph

Nurse at the El Salvador Rural Health Unit, Misamis Occidental, gives prescribed medication to sick baby.

ICA photograph

The largest number of rural health unit personnel were trained at the Quezon City Rural Health and Demonstration Center, a part of the rural health program in the Philippines. Here, the center's project director illustrates its scope and functions.

tion of the province. Often, where other organizations were inactive, his own local activities offered the sole medical services to the community. He apparently had no official control over the puericulture centers and essentially none over the various specialized programs.

In 1954, the bureau of health had 402 physicians, 152 nurses, 15 midwives, and 1,478 sanitary inspectors in the rural areas. With the 450 charity clinics operated by the bureau of hospitals and 500 active puericulture centers, there were an additional 880 physicians, 1,185 nurses, and 295 midwives employed at least part time in the rural areas.

Professional Health Workers

The duties of the sanitary inspector cover a wider field of activity than they do in the United States. In the Philippines, the sanitary inspector is an all-round health worker. He gives first aid and immunizations, makes sanitary surveys, diagnoses and treats disease, and fills out birth, death, and morbidity certificates. There is one stationed in more than 90 percent of the country's municipalities. In many areas, he is the first and only official health worker and sometimes the only government worker of any type. Educational requirements are high school graduation, and, before 1954, training was by the apprentice method. He still favors the khaki uniform with appropriate insignia and assumes the "parade rest" posture when in the presence of health officers, suggesting the quasi-military background of his specialty.

Midwifery is fairly well advanced in the Philippines, though there are many opportunities for improvement. In order to receive a license from the Board of Medical Examiners, the applicant must have completed an 18 months' course in a school approved by the government and have actually performed a specified number of deliveries under supervision.

Schools of nursing also leave something to be desired but are generally very acceptable. A bachelor's degree in public health nursing is offered by the University of the Philippines, and nurses were recently admitted to the Institute of Hygiene, the government university's postgraduate school of public health.

Physicians and engineers receive good specialty training in public health in the institute, which grants the certificate of public health and, provided a specified grade is maintained and a thesis approved, the degree of master of public health. Approximately 50 students are graduated each year, about 40 of whom are physicians. The faculty is well trained, and visiting teachers are provided by Johns Hopkins University under sponsorship of the Rockefeller Foundation and by the U. S. International Cooperation Administration.

Rural Population

According to an official estimate, the population of the Philippines in 1956 was 22,265,330. Of the three general areas in the Republic, Luzon Island is the most densely populated. Next in population density is the central or Visayan group of many smaller islands, and last is Mindanao Island. Palawan and Mindanao Islands, with the most acreage of essentially uninhabited land, are the main areas involved in the resettlement area program of the government.

The Filipino is predominately a rural citizen. At least 70 percent of the people live in rural areas and engage in predominately agricultural occupations. The 53 provinces are subdivided into municipalities, the basic government units, and the seat of municipal government is in the *poblacion*, situated where the population is densest. Elected officials of the municipality are a mayor, council members, a treasurer, police, and justice of the peace. Frequently the *poblacion* is also the site of an ancient church constructed during the Spanish regime. Scattered throughout the remainder of the municipality are more or less clearly defined subdivisions known as *barrios*. These are governed by a *teniente* or community leader, who is elected in some cases but who usually serves without pay, and a *barrio* council. An even smaller division is the *sitio*, hardly more than a collection of houses. The following illustrates the population levels of the municipalities according to the census of 1948:

Population groups	*Number of municipalities*
Under 5,000	206
5,000–20,000	691
20,000–40,000	229
40,000 and over	56

Another geographic division is the municipal district, which is administered entirely by appointed officials and has less autonomy than a municipality.

A peculiarity of the country is the large expanse of some of its 27 cities. Some of these have large areas that are definitely rural. One is said to be larger in area than any other city in the world, and another has parts which, until recently, were unexplored. The cities have their own government separate from the provincial administration.

Medical and Auxiliary Personnel

The distribution of medical and auxiliary personnel is predominantly urban. In July 1955, physicians in Manila and other urban areas numbered 4,996 out of an estimated population of 6 million, while the estimated rural population of 15 million had only 3,331. The number of medical school graduates examined annually by the Board of Medical Examiners more than quadrupled (249 to 1,050) between 1949 and 1954.

In 1954 there were 3,030 graduate nurses active in the country, a ratio of 1 : 5,400 of population. The ratio ranged from 1 : 940 in Manila to 1 : 26,972 in one of the provinces. Seventeen provinces had less than 1 nurse for each 10,000 persons. During the 5-year period 1950–54 a total of 2,533 nurses were licensed by the National Board of Nurse Examiners. There were 2,167 inactive nurses in April 1954. In the same month, there were 1,173 registered midwives, 287 of whom were in Manila.

Morbidity

As with most nations of Malayan ancestry, pulmonary tuberculosis is an important problem in the Philippines. The tropical climate

ICA photograph

ICA nursing consultant and her counterpart, a Filipino rural health nurse, make a home visit to a rural home in Tala, Rizal.

contributed much to the role of malaria as a leading cause of morbidity and mortality, but fortunately this disease is rapidly disappearing as the result of a successful residual spray program. Because of poor sanitation, the enteritides and schistosomiasis continue to be prevalent. The Philippines is the second most important endemic area in the world for *Schistosoma japonicum*; and, particularly among children, yaws, dermatophytoses, scabies, and "tropical ulcer" are common. Also, the effect of poor food habits and relatively low standards of living have contributed to the reported high incidence of nutritional deficiencies.

Campaigns against highly epidemic diseases, such as cholera and smallpox, have been successful. Small outbreaks have occurred, but no significant incidence has been reported for many years. The last recorded case of smallpox was in 1949, and of cholera, in 1935.

Apropos of this is the quality of mortality and morbidity reporting which leaves much to be desired. Reports from rural areas have been, in a high percentage of cases, from nonmedical personnel or from physicians who have never seen the cases.

High infant mortality, presumably related to poor obstetrical care, poor sanitation and nutrition, is another public health problem. In 1953 more than one-fourth (29.9 percent) of the deaths in the Philippines occurred below age 1, and more than one-half (53.5 percent) below age 3. Most deliveries are performed by the traditional birth attendant, or *hilot*, an unlicensed, untrained midwife. Informal reports of the percentage of deliveries by *hilots* range around 85 percent. Estimates of the proportion of deliveries by licensed midwives and nurses are about 10 percent, and by physicians, 5 percent. Hospitals usually take care of only abnormal deliveries, most women preferring to be delivered at home.

Philippine-American Demonstration

Following the establishment of the first mission of the U. S. Mutual Security Agency to the Philippines in 1951, the Department of Health made numerous studies of the health situation in cooperation with the Health Division of the mission. In 1952 the rural health unit project was formed. This project concentrated on a demonstration of integrated health services at the municipal level and provided a team of professional health workers for the demonstration. In most instances, communities without puericulture centers or charity clinics were chosen as sites for the demonstration. Teams of Filipino professional health workers, each consisting of a physician, public health nurse, midwife, and a sanitary inspector, were employed by the Department of Health with funds from the Philippine Council for United States Aid, and assigned to 81 municipalities. The U. S. Mutual Security Agency contributed equipment and supplies to the project. Each unit received a jeep, refrigerator, instrument sterilizer, microsope, examining tables, various medical instruments, and a supply of medicine calculated to last a year. These units were put into the field in 1953. In the subsequent year, additional units were set up in 52 sanitary district offices.

By the end of fiscal year 1954–55, a total of 244 units had been built up to a basic staff of 4 and given necessary equipment. Concurrently with the inception of this project, a training program was set up for the orientation of incoming personnel. Training centers were founded in four major cities of the Philippines. Also, the Rural Health Demonstration and Training Center in Quezon City was utilized. The orientation course, lasting about 6 weeks, consisted of a general review of public health programs, the organization of the department of health, and various administrative procedures in the conduct of local health services.

The *barrio* medical kit was an early feature of this rural health program. Its purpose is to furnish prompt medical care to the isolated *barrio* during the interim when more comprehensive phases of the rural health program are being organized. Essentially, the kit is a large plywood case containing a supply of relatively simple drugs and remedies which could be used with a minimum of medical supervision. Accompanying it is a manual covering basic sanitation, nutrition, health education, first aid, and emergency treatment of common conditions found in rural areas. The kit is preferably placed in a new hut or a house specially constructed of local materials, but sometimes the residence of a prominent citizen is satisfactory.

The kit is administered by a *barrio* health committee of from 3 to 5 members, usually including a teacher and a sanitary inspector, if one is stationed in the area. Supervision is assigned to the municipal health officer. Usually, the provincial health officer is also particularly interested in the project and assists in its organization and supervision.

Local health services have been assisted by the United Nations Children's Fund, mainly in the form of support of special programs, including maternal and child hygiene, yaws control, and BCG vaccination.

The Rural Health Act of 1954

In July 1954, the Congress of the Philippines passed the Rural Health Act, calling for the establishment of a rural health unit in every municipality and municipal district of the Philippines. It also made several administrative changes in the rural health program, among them the appointment of municipal health officers, the changing of the name of the district health officer to provincial health officer, the establishment of dental services in each congressional district, and the general increase in salaries of local health personnel. It also appropriated for this program 4 million pesos ($2 million, at the official rate) plus 1 million pesos annually for 4 years. The target date for full application of the act is July 1958.

The act called for two categories of units, a senior unit of a physician, public health nurse, midwife, and sanitary inspector; and a junior unit with a combination of a physician or a nurse plus a midwife or a sanitary inspector. Every municipality or combination of municipal districts with a population of more than

Status of rural health units relative to staffing projected under the Rural Health Act

Fiscal year	Total units in operation at end of fiscal year (complete and incomplete)	Junior units		Senior units			
		Cumulative total completed	New units completed	Cumulative total completed	New units completed	Raised to complete units [1]	Incomplete units
1955	1,000	----------	----------	650	----------	----------	350
1956	1,100	66	66	801	34	117	233
1957	1,200	132	66	952	34	117	116
1958	1,300	198	66	1,102	34	116	----------

[1] To be raised to complete staff of four members before end of fiscal year.

5,000 was to receive a senior unit. Those of more than 35,000 were given a junior unit in addition.

An additional provision established a public health dentist in each congressional district, those with more than 150,000 population receiving an additional dentist. This was estimated to provide 162 dentists for the 102 congressional districts. Dental positions already in the public health programs were included in this total figure. This program has been developing slowly, and funds for travel and for equipment have been increased to accelerate its progress.

The Rural Health Act also set up the following new scale of salaries for local health personnel:

Position	*Range*
Municipal health officer	₱3,000–4,200
Public health dentist	2,400–3,120
Public health nurse	2,400–2,580
Midwife	1,440–1,800
Provincial sanitary inspector	1,440–1,560

These salaries may be compared with the wages of private corporation employees compiled in a survey made for the Wage and Position Classification Office of the Philippine Government in 1954. These salaries apply to urban areas only:

Position	*Interquartile range*
Physician	₱2,092–5,550
Dentist	1,515–4,000
Nurse (hospital)	1,266–1,785
Hospital attendant	1,075–1,238

To fulfill the project in an orderly manner, a plan of operation was drawn up in 1954 in which the rural health units gradually progress towards the complete staffing called for in the act (see table).

As of July 1, 1956, the project was proceeding well, even a little ahead of schedule. The following is an analysis of the staffing of rural health units on that day in 1,317 municipalities and municipal districts, in reference to the projected plan:

Number with all four categories filled	510
Percent with all four categories filled	38.8
Number with three or more categories filled	876
Percent with three or more categories filled	66.6
Number with health personnel of any category	1,231
Percent with health personnel of any category	93.5
Number of physicians on duty	1,013
Number of nurses on duty	814
Number of midwives on duty	855
Number of sanitary inspectors on duty	1,491

Usefulness of Equipment

At the end of 1953, the 81 demonstration units were polled on their use of the various items of equipment. Among the items listed as most useful were the jeep, the outboard motor, the sphygmomanometer, stethoscope, microscope, examining table and chairs, and refrigerator. The following are the results of the poll, in general, and some observations made by unit personnel and consultants.

The most useful piece of equipment, according to 66 of the 81 units, was the jeep. Where any reasonable semblance of road existed, it increased the effective range of health unit personnel in their assigned areas. In most rural sections, automotive transportation, public or private, was still scarce. The jeep was used not only to transport unit personnel to the peo-

ple but also to carry patients to the hospital. It mobilized the unit. There were, however, few facilities for repair and maintenance in most rural areas. Also, since automobiles were relatively scarce in most of these areas, even among government officials, the jeep was subject to unauthorized use. In addition, relatively few Filipinos had been trained to drive or properly maintain automotive equipment. Solutions were being found to most of the problems, however, through revision of antiquated rules and regulations, training of personnel, and the maximum use of district engineer stations or vocational training schools.

Particularly useful in the Philippines for serving the more than 600 inhabited islands were outboard motors. Usually, the small islands are settled only along their coasts and since few or no roads exist inland, transportation must be by water, either on rivers or the open sea. Frequently, one municipality includes several small islands to which no public transportation is available. Motors were used to propel the traditional *banca* type of boat which could be maneuvered close to shore and which, when equipped with outrigging and a 25 hp. motor, could successfully negotiate stretches of open water. The same problems of supply and maintenance applied here but were not so large.

The original 81 demonstration units reported the sphygmomanometer and stethoscope to be the second most useful items. They were used extensively by physician, nurse, and midwife in maternal and child hygiene work. Most of these mercury type sphygmomanometers that were supplied apparently were in good condition after 3 years.

The original justification for the typewriter was for typing of records, reports, and correspondence. Correspondence was minimal, however, and many records were handwritten. There was considerable doubt that the usefulness of this item for persons not particularly trained in its use justified its relatively high cost.

The use of the microscope was mainly confined to the examination of urine (a small hand centrifuge was also supplied) and of feces for parasite ova. Blood smears for malaria were examined occasionally and blood counts infrequently. The general opinion was that the microscope should be issued only to physicians who could be expected to use it efficiently. Fungus growth on the lens and some rust or corrosion were noted but less than expected in the tropical climate. Few facilities existed in the Philippines for repair and maintenance of microscopes.

For emergency and minor surgery, the original units were supplied with 12 mosquito forceps, 24 hemostats, 4 tissue forceps, 4 dressing forceps, 2 sponge forceps, 2 needle holders, 6 surgical scissors, and 2 grooved directors. Also included were an ether mask, an ether dropper, and rubber gloves. It was found that after 2 years of operation very few units had used more than 1 or 2 of the instruments. In many units most of the forceps were never removed from the original package. The ether mask and dropper were not known to have been used in any unit, and the rubber gloves in many instances had deteriorated. Rural health units were doing little more than repair of superficial lacerations or other very minor surgery; the equipment originally given exceeded actual needs, except for obstetrical forceps which were used by many units. Rural physicians evidently preferred to transport seriously injured or ill patients to the hospital than to operate under unfavorable conditions, especially if they did not have special training or experience in surgical procedures. Also, the hospital system in the Philippines was fairly well developed, there being at least one government hospital in every province.

The use of the refrigerator in rural health units has been mainly for storage of biologics, antibiotics, and perishable drugs. Few blood and urine specimens, water samples, or other materials for examination were stored in refrigerators, probably because the proposed system of regional laboratories had not been sufficiently developed to handle such work from the average health unit. Refrigerators up to 7 cubic feet were placed in units, but they were much too large for the average 4- to 5-worker unit in the present stage of development. The small 1½ cubic foot refrigerators are being ordered. Problems of operation also plagued

the use of this item. Many small towns had no electric current or had it only for varying periods of 6 to 12 hours a day. However, if the full capacity of the freezing unit were used to freeze ice during the time the unit was in operation, the box would be cool during the nonoperating period. Another apparently successful alternative was the kerosene refrigerator. Kerosene was usually available in the rural areas, and, when properly operated, this type of refrigerator seemed to function well in tropical climate.

The simply constructed metal examining tables and chairs were undoubtedly in use, as was other furniture supplied by the Philippine Department of Health. After much evidence that these items could be constructed locally from native materials, it was decided to foster this approach to stimulate interest in the health unit and its work. Such tables and chairs were frequently donated by individuals, with credit plainly lettered on the piece. Sample plans and bills of materials were supplied to local health officers. The items will therefore probably not be supplied to the Philippine rural health program by international assistance agencies in the future.

Electric and alcohol sterilizers were supplied, as well as pans for use on primus stoves. The same difficulty was found with the electric sterilizer as with other electric appliances. Sterilizing instruments was possible at night when current was available but the unit personnel were not anxious to do the job then; they preferred to find other methods that could be used during the day. The large alcohol sterilizer needed a large amount of fuel to bring the necessary amount of water to a boil. Usually, it was used only to sterilize the larger instruments such as obstetrical forceps. The small alcohol syringe and needle sterilizer was useful in smaller clinics.

Conclusion

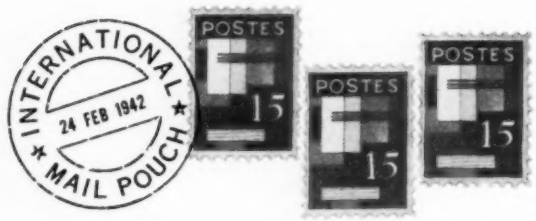
The background and salient points in the evolution and progress of local health services in the Republic of the Philippines have been presented with the expectation that the problems in that country are parallel with those in other countries in the area. Opportunities will arise in the future for exchange of information on the application of the Philippine program. One thing is certain: The rural people in the Philippines want these services, and the demand is large and steadily augmenting.

Tenth World Health Assembly

Surgeon General Burney headed the United States delegation at the Tenth World Health Assembly in Geneva, May 7–24, 1957. Highlights of the assembly were adoption of the 1958 budget of $13,500,000 recommended by the executive board and unanimous acceptance of the invitation to hold the eleventh assembly in the United States. The U.S.S.R., Albania, Bulgaria, and Poland resumed active membership.

In addition to calling for more voluntary contributions to the special malaria eradication fund, the assembly approved a continuing WHO program in peaceful uses of atomic energy. This program includes training health physicists and physicians in public health aspects of atomic energy, scheduling an expert committee meeting on graduate public health training in atomic energy, and study of disposal of radioactive wastes.

Dr. Al-Wahbi of Iraq, president of the assembly, awarded the Darling Foundation Medal and Prize to Dr. Paul F. Russell of the Rockefeller Foundation for outstanding achievements in the control of malaria. The Leon Bernard Foundation Prize was awarded to Professor Kacprzak of Poland for his work in social medicine.



These paragraphs, based on overseas reports from public health personnel with missions and field parties of the International Cooperation Administration, give a glimpse into health work abroad. Most of the original material appears in an administrative publication distributed by the Public Health Division of the ICA.

Plaque for Sulimaniyah

The new health center of Sulimaniyah in Iraq received a silver plaque in honor of its part in the agriculture and industry exhibition held for the first time in that place. Visitors from town and village were received at the center with complete explanations of the uses of this facility. Sulimaniyah has been isolated from external influences. The economy is rural, the faith Islamic (Sunni sect), the language Kurdish (many dialects). Most Kurds also speak some Turkish, Farsi, or Arabic. Those who have been to school read, write, and speak Arabic and Kurdish and frequently have some understanding of English.

—M. Elizabeth Darden, *public health nurse adviser, formerly with United States Operations Mission, Iraq.*

Smallpox Detection the Hard Way

On the afternoon of December 13 we received a report of smallpox in the village of Pishvah 45 miles southeast of Teheran in the Varamin area of Iran. Dr. Cyrus Arasteh and I readied an investigation team and vehicle and departed that night, in a mixture of snow and drizzle. We came to a flooded river where we charged with our 4-wheel drive around a bus and a large truck that were stuck side by side blocking the "road." But we mired in over the hubs and slammed against a high bank. Our hardy Iranian driver, Akbar, took off his shoes, rolled up his pants legs to the hip, jumped out in the falling snow and icy water, and began digging furiously, singing gaily the whole time. An hour and a half later with the help of a cable to another car we wound ourselves up out of the sea of mud. In the meantime my efforts to help had amounted to my stepping off into space of the black night for a 6-foot fall into a ravine where I ended up with muddy water over my head. I had some damage to my knee and was litter bound for the rest of the night. During our investigation three cases of smallpox were found in a family that had recently arrived from Tabriz. Nine thousand persons in the area were vaccinated, and it was reported that no more smallpox occurred.

A tiny Iranian gets immunized against smallpox in Iran's national campaign against the disease by one of the vaccinators trained by the International Cooperation Administration for the program.

—Franz Rosa, M.D., *public health physician, United States Operations Mission, Iran.*

Endowment

In a village near Shiraz, Iran, the year-long efforts of a sanitary aide with the Public Health Cooperative Organization to build a sanitary program reaped an unexpected benefit. One of the villagers, who owned a small amount of property, became so impressed with what he had learned about sanitation and hygiene that he endowed the rent from one of his shops to the village council for sanitation in the village.

—Albert P. Knight, M.D., *chief, Health Division, United States Operations Mission, Iran*

Characteristics of Large Medical Expenses

SELMA MUSHKIN, Ph.D.

Urban families spending $1,000 or more for medical care in 1950 devoted a far larger share of their medical dollar to hospital and nursing services than did the average urban family. In more than 4 out of 5 of these families at least one member was hospitalized during the year. For these members the average length of hospital stay was about 27 days, as compared with an average stay in all short-term hospitals in 1950 of 8.1 days.

The $1,000 or more out-of-pocket medical expense was usually attributable to the medical care spending of a single family member. Again in more than 4 out of 5 families there was a single member with a medical care outlay of $500 or more. The remaining families fall about equally into two groups, large families with expenditures of $200 or more for several individuals in the family and small families with two or more members with expenses totaling $500 or more.

CURRENT interest in major medical insurance has focused attention on families who in any single year incur heavy medical expenses. A number of questions have been raised about the composition and characteristics of such expenses. To provide some answers to these questions, the Public Health Service has studied a stratified subsample of schedules of family income and expenditures obtained by the Bureau of Labor Statistics in its 1950 survey of spending habits of urban consumers.

In all, only 1.3 percent of urban families reported out-of-pocket medical care expenditures of $1,000 or more, including premiums paid for voluntary health insurance but excluding the value of any benefits received. This percentage is the equivalent of about 400,000 urban families, with 1.4 million family members. Medical care expenses of these families, however, totaled about $655 million, or about 10.6 percent of the estimated $6.2 billion total out-of-pocket expenses of urban families. Of this $655 million, about two-thirds was spent by families with medical care costs of $1,000 to $2,000 and one-third, by those spending $2,000 or more.

Study Methods

The methodology of the Bureau of Labor Statistics survey and that of the Public Health Service special study of a stratified subsample of the schedules obtained in this survey were summarized in an earlier report (*1*). The subsample used in the special study included some 2,414 consumer units (and 7,639 persons) out of the total 12,489 consumer units interviewed by the Bureau of Labor Statistics. It included, however, all schedules on which out-of-pocket medical care costs of $1,000 or more were reported by the family. In all, there were 165 consumer units, composed of 553 persons, in the $1,000-or-more category. Information from these schedules was weighted to adjust for the regional variation in sampling ratios. The tabulated figures adjusted in accordance with weights developed by the Bureau of Labor Statistics form the basis of the estimates presented here.

Use of a sample of this size necessarily involves considerable random error due to sampling. In this survey, there are additional important sources of error in that a single family respondent may have reported family expendi-

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431430—57——3

tures for all family members and reports were made for the entire preceding year.

Types of Services

What types of health services are purchased by families spending $1,000 or more?

The medical care bills of families spending $1,000 or more have a very different health service content from that of the average urban family's medical bill. A far larger than average portion of their out-of-pocket medical expenses goes for hospital services and for special duty nursing. A smaller than average portion represents payments for dental services and for drugs.

While the average urban family spends about 12 cents of its medical out-of-pocket dollar for hospitalization (excluding services paid or reimbursed by voluntary insurance plans and those publicly financed), families with bills of $1,000 or more spend more than 30 cents of their medical dollar for hospital services. Special duty nursing, which accounts for only 2 cents of each $1 spent for medical care for all urban families, represents 14 cents of each $1 of out-of-pocket medical expense for families with medical bills of $1,000 or more. The average expenditure for special nursing services for these families exceeds the total amount spent for all medical care by the average urban family (table 1).

Within these averages there is a wide variation in distribution of out-of-pocket medical costs among classes of health services. This variation depends upon such factors as the nature of the illness, the level of family income, the size of the family and other family circumstances, entitlement to care under public or other programs, and eligibility for benefits under health insurance plans. About 8 out of each 10 families spending $1,000 or more report at least one episode of hospitalization during the year. In some instances the expense of the hospitalized illness, including both hospital bill and physician services, accounts for a large share of the total family medical care expenditure. Length of hospital stay averages approximately 27 days for these hospitalized family members, as compared with an average length of stay in short-term general and special hospitals for the whole United States population in 1950 of 8.1 days (*2*). (In assessing these lengths of stay, account must be taken of the fact that some long-term hospital care is included in the Bureau of Labor Statistics schedule information.)

Table 1. Distribution of annual out-of-pocket medical expenses, by type of health service, for all urban families and families with medical expenditures of $1,000 or more, 1950

Type of service	All families [1]		Families spending $1,000 or more	
	Average	Percent	Average	Percent
Total	$197	100.0	$1,573	100.0
Insurance premiums	34	17.3	55	3.5
Physicians	63	32.0	489	31.1
Hospitals	23	11.7	491	31.2
Dentists	30	15.2	110	7.0
Nurses	4	2.1	218	13.9
Drugs	28	14.3	122	7.7
All other	15	7.4	88	5.6

[1] Data for all urban families based on Bureau of Labor Statistics tabulations of entire sample, rather than Public Health Service subsample.

However, there are some families with $1,000 or more of out-of-pocket expenses in which no member of the family was hospitalized during 1950. As may be expected, physicians' services in the home or office account for the largest part of nonhospitalized illness expense. For approximately 5 percent of the families special nursing costs account for more than 66⅔ percent of out-of-pocket medical care expenditures. Dental services in some instances account for one-third or more of out-of-pocket expenses and range up to $1,000 for individual families. These less frequent but nevertheless significant deviations from average medical expense burdens point to the need for broadening prepayment arrangements to encompass the broad range of services purchased by urban families (*3*, *4*).

Expenditures of Individual Family Members

Are large family medical expenses the result of a single expensive illness or are they the ac-

cumulation of sizable expenses for several family members?

The largest portion of urban families with out-of-pocket expenses of $1,000 or more—almost 87 percent—reported outlays of $500 or more for a single family member. For about 7 percent of the families there were 2 or more family members each with $500 or more in medical care expenditures. The remaining families spending $1,000 or more were relatively large families that had no member with medical expenses of as much as $500 during the year.

While family expenditures of $1,000 or more during a year appear to be primarily attributable to the expense of a single member of the family, it is important to note that about 47 percent of all members of these families spend at least $200, which is more than 3 times the amount spent by the average urban resident. Similarly, about half of these families had 2 or more members with medical care expenditures of at least $200.

The distribution of expenditures of members of families spending $1,000 or more for medical care differs markedly from the distribution of amounts spent for medical care by the urban population as a whole (table 2). While 65 percent of the urban population report expenses of less than $50 a year, only 25 percent of the persons in families spending $1,000 or more report expenditures in this range. Almost 30 percent of the persons in these families spend $500 or more.

Table 2. Percentage distribution of all urban residents and persons in urban families with medical expenditures of $1,000 or more, by total out-of-pocket medical care expenditures, 1950

Out-of-pocket medical care expenditures	Percent of all urban residents	Percent of persons in families spending $1,000 or more
Total	100. 0	100. 0
None	17. 4	6. 0
$1–$49.99	47. 9	19. 3
$50–$99.99	17. 5	16. 2
$100–$199.99	10. 2	11. 8
$200–$299.99	3. 7	8. 0
$300–$499.99	2. 1	8. 9
$500–$999.99	1. 0	12. 8
$1,000 and over	. 2	17. 0

Table 3. Percentage distribution of all urban families and of urban families with medical expenditures of $1,000 or more, by income class, 1950

Income class	Percent of all urban families[1]	Percent of urban families spending $1,000 or more
All income groups	100. 0	100. 0
Under $2,000	18. 6	6. 6
$2,000–$3,999	42. 7	30. 2
$4,000–$5,999	26. 3	24. 3
$6,000 and over	12. 4	38. 9

[1] Data for all urban families based on Bureau of Labor Statistics tabulation of entire sample, rather than Public Health Service subsample.

Two important factors associated with these variations in patterns of spending, apart from differences in illness experience and in utilization of medical services, are family income and age of family members.

The average city family spends about 5 percent of its $4,000 income after taxes for medical care (*1*). Urban families spending $1,000 or more for medical care have an average income of nearly $7,000, but more than 20 percent of their income goes for medical care. However, the individual schedules for these families show a great variation in income (table 3) and in the percent of income spent for medical care. Medical expenses vary from about 3 percent of current income to many times current income.

Families with large medical care bills have a lower proportion of children and a higher proportion of older people than the average urban consumer unit. About one-third of the urban population in the Bureau of Labor Statistics sample are under 19 years of age, whereas only about one-quarter of the persons in families spending $1,000 or more are in this age group. Also, there is a smaller percentage of persons aged 19–44 years in families spending at least $1,000 than in the urban population as a whole. The percentage of people aged

Table 4. Percentage distribution of all urban residents and of persons in urban families spending $1,000 or more for medical care, by age group, 1950

Age group (years)	Percent of all urban residents	Percent of persons in urban families spending $1,000 or more
All ages	100. 0	100. 0
Under 6	12. 7	8. 7
6–18	19. 1	15. 7
19–44	38. 3	28. 0
45–64	21. 3	33. 4
65 and over	8. 6	14. 2

45 or over, however, is approximately half again as great in families spending $1,000 as in the total urban population (table 4).

Voluntary Health Insurance Coverage

Are members of families with large medical bills covered under health insurance plans?

While families with large medical expense have higher than average incomes and include a larger than average proportion of older persons, they have about the same voluntary health insurance coverage as other families, measuring coverage only in terms of whether or not there is some participation in health insurance plans. The proportion of persons covered in each age group is approximately the same for all urban residents as for persons in families spending more than $1,000 (table 5). For all ages combined, about 6 out of 10 persons are covered. In the older age groups, for all urban families as well as for families spending at least $1,000 for medical care, the proportion covered is significantly lower than for younger age groups. Approximately 2 out of 6 persons aged 65 years or over in all urban families and about 2 out of 5 persons in this age group in families spending $1,000 or more have some health insurance coverage. This finding of a decreasing proportion of coverage among the older age groups for urban residents parallels the data published in other studies, including the recent nationwide study of the Health Information Foundation (*5,6,7a*). The Health Information Foundation found that in 1952–53, 57 percent of persons of all ages had hospital insurance; the proportion of persons covered declined to 54 percent in the age group 55–64 years and to 31 percent in the age group 65 years and over. The Health Information Foundation study includes rural as well as urban groups and relates to a later year.

The health insurance benefits for which members of families spending $1,000 or more were eligible were patently not sufficiently broad in scope to cover the variety of medical services needed by these families. Health insurance coverage of those members who experienced a hospitalized illness was about the same as the coverage of all other members of the families spending $1,000 or more and similar to the coverage of the urban population as a whole. About 56 percent of the members with hospitalized illnesses were covered under a health insurance plan. While data on amounts of health insurance benefits reported on the Bureau of Labor Statistics schedules are inadequate because of the volume of nonreporting, benefits shown on schedules (for which reports were made) averaged about 30 percent of the cost of the hospitalized illness. Included in this average are the cost of physician services, nursing care, and other expenses, as well as hospital charges. It must be remembered that interviewers of the Bureau of Labor Statistics

Table 5. Percentage of all urban residents and of persons in urban families with medical care expenditures of $1,000 or more with some health insurance coverage, by age group, 1950

Age group (years)	Percent of all urban residents	Percent of persons in families spending $1,000 or more
All ages	60. 7	60. 9
Under 6	59. 1	57. 2
6–18	60. 8	66. 3
19–44	65. 3	66. 7
45–64	62. 4	62. 8
65 and over	36. 6	41. 3
65–74	41. 8	----
75 and over	25. 7	----

Distribution of Aggregate Medical Care Expenditures

The distribution of out-of-pocket medical care expenses of urban families in 1950 by class of service is compared with similar information from other sources in the accompanying tabular summary.

The Bureau of Labor Statistics survey findings are comparable to the distribution derived for out-of-pocket medical expense by the Health Information Foundation in its 1952–53 study. Differences between these data and other series are attributable primarily to the dissimilarity in definition of medical expense.

The Department of Commerce figures and the derived Social Security Administration estimates of personal medical care expenditures on which distributions usually published are based show gross private expenditures, including expenditures financed by families, by insurance plans, and, in some instances, by employers. The Bureau of Labor Statistics data presented here represent only family out-of-pocket expenses and exclude health insurance benefits received from the various plans and payments made directly or indirectly (through insurance plans) by employers. There are many other conceptual differences in the figures. Several preliminary analyses have been made which detail the differences between a household survey estimate of medical expenses and the national aggregate estimates as prepared currently by the Department of Commerce (*7b, 12–14*).

Comparison of percentage distributions of medical care expenditures by type of service [1]

Type of service	Bureau of Labor Statistics	Health Information Foundation	Department of Commerce	Social Security Administration	
	Out-of-pocket expense [2]		Gross costs [3]		
Total	100	100	100	100	100
Physicians	39	38	37	32	32
Hospitals	14	12	20	26	27
Dentists	18	18	16	11	11
Drugs	17	17	15	18	18
Other	12	15	13	13	12

[1] Data relate to 1950, except the Health Information Foundation survey findings, which are for 1952–53.
[2] Excluding health insurance premiums paid.
[3] Excluding administrative and other net costs of health insurance coverage; including benefits paid by health insurance plans.
SOURCE: References 7c, 15, 16, and 17.

were concerned principally with out-of-pocket expense for the whole gamut of consumer goods and services and not with collecting the supplementary data included on the schedule.

Prepayment for medical care expense may be expected to change the shape of the distribution curve of medical expense. The percentage of families with large medical expense, for example, should be lower today than prior to the growth of voluntary health insurance. Voluntary health insurance premiums, on the one hand, and benefits provided, on the other, should have evened out the distribution of medical spending and reduced the incidence of the large medical bill. Many other changes—demographic, scientific, economic, and institutional—have influenced the distribution of families by size of medical expense. Differences in design and scope of survey and in definition and size of family units, as well as sampling errors, particularly at the tail of the distribution for expenses of $1,000 or more, however, make it difficult to compare 1928–31 findings of the Committee on the Costs of Medical Care and later family surveys (*8, 9*).

A crude analysis of the trends since 1928–31 points to the need for additional study of the change in importance of the large medical expense. Two questions in particular are suggested. Has the cost of major illness increased more than average family expense for medical care? Has the relative number of expensive illnesses decreased? There are a number of trends which affect medical care outlays in diverse ways. For example, costs of care for some types of illness are lower today than 25 years ago because of changes in the incidence and severity of these illnesses and changes in methods of treatment which involve shorter hospital stays, use of antibiotics, and other new

drug therapies (*10*, *11*). However, improved medical procedures and therapies make for higher costs of care for other major illnesses, and the aging of the population increases the frequency of these illnesses.

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Health Survey in the Great Plains Area

Extensive study by the Public Health Service of health needs in sparsely settled rural areas started July 1, 1957, with a survey of the health situation in Kit Carson County, Colo. Counties in the Great Plains area have been selected for the study because there are few local health departments in that area to serve the widely scattered farm population, and because farm incomes there have been affected adversely by drought and other severe weather variations.

The Kit Carson study will cover more than 1,500 families, with cooperation from the Colorado State Department of Public Health, local physicians, and county leaders.

Tuberculosis Prophylaxis Trials in Preview

SHIRLEY H. FEREBEE, FRANK W. MOUNT, M.D., and CARROLL E. PALMER, M.D.

SINCE 1952 the drug isoniazid has been used widely and effectively in the treatment of tuberculosis. This demonstrated effectiveness in treatment has led to the idea that isoniazid may be effective as a prophylactic agent.

To say that isoniazid prophylaxis of tuberculosis is controversial is certainly not to exaggerate. Some believe it can prevent tuberculous infection from progressing to clinical disease or can even prevent infection itself. Others just as firmly believe it can prevent neither infection nor disease but instead will interfere with the acquisition of resistance. On the basis of these beliefs, the use of prophylactic isoniazid is either advocated or opposed.

Both these beliefs are based on analogy. Advocates draw support for their view from the results of the treatment of patients. Opponents base their position on animal experiments. No direct evidence of the effectiveness of isoniazid prophylaxis in human beings has yet been produced.

The Public Health Service finds itself unwilling, without direct evidence, to endorse the prophylactic use of isoniazid. It is equally unwilling, without direct evidence, to dismiss the possibility that isoniazid may be an effective prophylactic. In this dilemma, a program of carefully planned control studies involving large numbers of people seems the only solution. Consequently, the Public Health Service, with the cooperation of tuberculosis workers throughout the country, has initiated a series of prophylaxis trials.

The first of these trials was begun in January 1955. Its purpose is to see whether the frequency of complications of primary tuberculosis can be decreased by the prophylactic use of isoniazid. In this study, more than 2,500 children with asymptomatic primary tuberculosis are being observed in 31 pediatric clinics.

A second trial, in which local health departments are participating, is now getting under way. Health departments ordinarily keep under observation persons considered to be at greater than average risk of tuberculosis so that treatment can be started at the first sign of active disease. These persons are of two kinds: those whose risk is considered to be due to unusual exposure, that is, the household contacts of newly discovered cases of tuberculosis, and those who are considered at unusual risk because of suspicious pulmonary pathology observed on X-ray films but whose present condition does not require treatment.

For these "special risk" groups, the Public Health Service is helping health departments add the prophylaxis trial to their already established services. Household contacts make up the larger part of the study population. In addition to the usual "watchful waiting," half the persons in this trial are receiving daily isoniazid and the other half placebo.

Each participating health department tuberculin tests and X-rays the household contacts of each newly discovered case of pulmonary tuberculosis. Any contact with evidence of active tuberculosis is referred to his family physician or a tuberculosis clinic for treatment. The others are asked to enter the study.

The household is given a bottle containing a month's supply of enough pills for each adult member of the family to receive a daily dose of between 3 and 7 mg./kg. of body weight and for each child to receive a daily dose of between 5 and 10 mg./kg. Each month for the next 11 months, a member of the household picks up a new supply of pills at the health

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department and returns the previous month's bottle. The number of pills remaining in the bottle when it is returned is a clue to the regularity with which the family has been taking the pills.

At 3-month intervals during the year, a nurse from the health department visits the family and reports on the health of each family member the regularity with which the family is taking its pills, and the amount of time the member with tuberculosis has spent in the home.

At the end of the 12th month, the household members are reexamined in the clinic with tuberculin tests and X-rays.

The procedure is essentially the same for the tuberculosis suspects, except that the suspect, rather than his family, is the study member.

During the year each health department continues its usual observation of these tuberculosis suspects and household contacts. If one of them develops clinical tuberculosis, he is removed from the assigned medication and referred to his physician or tuberculosis clinic for treatment. The other members of the family continue to receive the assigned medication.

While this scheme is simple for any one household, its application to many households in a number of cities creates administrative problems for the central office in Washington. Most of the difficulties stem from our determination to make the observations as objective as possible. We believe it is critical that neither those who are taking pills nor those who are observing them should know whether a household is receiving isoniazid or placebo. Households receiving placebo must have the same faith in the usefulness of their pills as those taking isoniazid. The public health nurses must watch those who are taking isoniazid with the same concern they feel for those taking placebo. The physician who diagnoses tuberculosis in a household contact must not be influenced by the knowledge that a person has or has not been receiving isoniazid. The only way to make sure that the study is free from bias is to make the two products indistinguishable and to tell no one outside the central office what each bottle contains.

Bottles of pills labeled only with code numbers are sent to the health departments. They are of the various sizes necessary to provide a month's supply of pills for families containing from 1 to 16 persons ranging from 2 months to more than 70 years of age. The health departments assign the initial bottles to the households and thereafter receive from the central office each month a new bottle for each family. The scheme is so arranged that half the households of each size receive isoniazid and the other half placebo.

It will not be known with any precision how faithfully people take their pills. The most we shall know is how many say they do, how many of them return each month for a new supply, and what the returned bottles indicate. If, at the end of the year, the isoniazid households should have as much tuberculosis as the placebo households, we would not know whether this is a failure of isoniazid or a failure to take the pills. But we would know that to distribute isoniazid as a prophylactic in the way it is being done in this study is not a useful tuberculosis control measure. If isoniazid households should have less tuberculosis than placebo households, we would know that this is a minimum difference, that prophylactic isoniazid is at least this effective. The inclusion of both positive and negative tuberculin reactors in the study population should provide a means of learning whether new infection can be prevented among the tuberculin negatives and whether new disease can be prevented among the tuberculin positives while isoniazid is being taken.

Each person will take pills for only 1 year, but he will be observed, at least at 6-month intervals, we hope, for a number of years. From this continued followup, we hope to gain some information as to whether isoniazid has any lasting effect on old infections and whether prophylaxis of the uninfected during exposure interferes with their resistance during subsequent exposure.

We recognize that the task of evaluating isoniazid as a prophylactic agent is formidable. Nevertheless, the consequences for the control of tuberculosis would be so tremendous should the drug prove effective, and the indirect evidence that it will work is so promising, that we feel obliged to try.

The R. E. Dyer Lecture

The Natural History of Plague and Psittacosis

KARL F. MEYER, M.D.

THE invitation to deliver the sixth R. E. Dyer Lecture is interpreted as an opportunity to appraise the past, present, and future of bacteriology and epidemiology in their relation to medicine. As the investigator honored by these lectures has so eminently shown, the study of infectious diseases still promises exciting discoveries, despite the advances of recent decades.

Immunization and antimicrobial therapy have certainly expanded man's control over many infections. Few who entered the fields of pathology and bacteriology 50 years ago could foresee the imminent reduction in the number of deaths from diphtheria, pneumococcal pneumonia, streptococcal infections, yellow fever, typhus, and plague. One keeps in mind the intelligence and devotion of those whose work made this reduction possible. Some of their work was brilliant; much more of it was simply intelligent. It was all invariably persistent.

The triumphant results of these efforts have led to the prevalent misapprehension that no one should now die of or even suffer inconvenience from an infection. The origin and consequences of this attitude are readily traceable from the success of chemotherapy of spirochetal and protozoan infection to the more dramatic experiences with sulfonamides and antimicrobial drugs. In many cases, chemotherapy has unquestionably eliminated the infector from the infected, allowing the infected to survive where once he would have perished. If a measure can preserve life, it may be unfair to point out its shortcomings, even its faults.

To comprehend the whole nature of the relationships of the new chemotherapeutic agents, the micro-organisms, and the infected human being is not so simple. Misleading simplifications abound in the minds of laymen and of physicians. But among microbiologists there is still much conjecture about the mode of action of these drugs.

The exceptional nature of the host-drug-parasite relationship is not always understood. Infectious agents do not characteristically submit to unconditional surrender. Throwing great quantities of every drug against every infection will insure only a steady decrease of satisfactory responses and a steady increase in toxic reactions, sensitized patients, and re-

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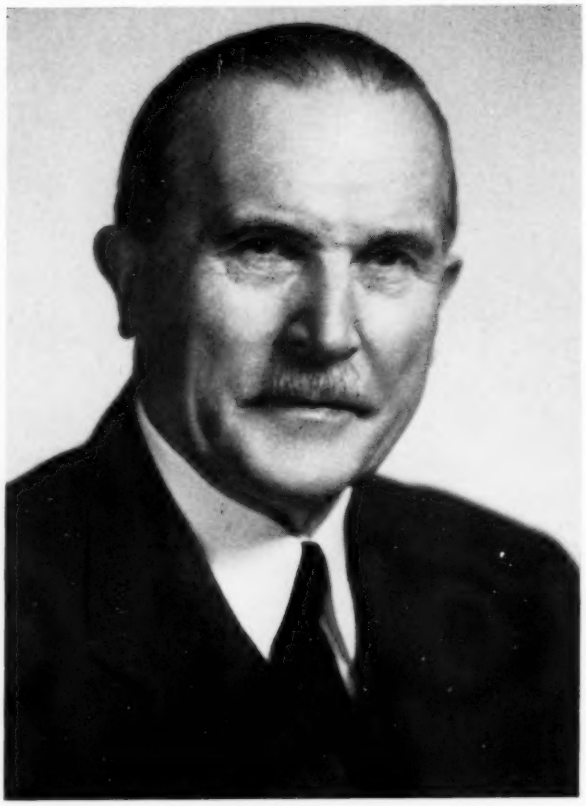
431430—57——4

sistant bacteria. It is now fairly well understood that insufficient amounts of the drugs may allow bacteria to survive treatment and that later the bacteria may multiply and cause a relapse. But it is not always understood that the organisms may not be easily reached by the drug and may therefore not be subjected to its adverse effects. Adequate elimination of the organisms may depend on continued administration of powerful drugs in large doses or on combined chemotherapy.

Use of the antimicrobials is not without dangers. To overlook or even deny the toxicity of some of the drugs leads to carelessness, misplaced enthusiasm, inevitable disappointment, and abuse of a useful tool. In order to use the extraordinary powers of the drugs to greatest advantage, one must recognize that some of the drugs are toxic, that they may lose their effect, and that they may even do harm unless those who administer them have a thorough understanding of bacteriology.

The dramatic early results of chemotherapy were not matters of chance. Fundamental research in bacteriology made the miracles possible, and day-to-day study has been necessary to keep them miraculous. When the new drugs were scarce, each patient to be treated was chosen with care and treatment was carefully controlled. This is an important reason why failures were few. Knowledge and understanding of the natural history and pathogenesis of infections must correct some of the grosser mistakes now being made. Adequately trained workers in good laboratories open to physicians in hospitals, in public health agencies, and in private practice are and will continue to be needed.

Other factors refute the prevailing view that infectious diseases have been conquered. These diseases have been significant through centuries, and they will continue to be so. The human race is condemned to coexistence with parasites. If they are underestimated they may regain their lost ground. The advances called to mind by the names Jenner, Pasteur, Lister, Koch, Roux, and Theobald Smith have altered the course of the infectious diseases quantitatively with respect to location and time. But the suppression of certain epidemic diseases in relatively small areas has in no way



Dr. Karl F. Meyer

influenced parasitism in general. The everlasting question, what forces create, maintain, and suppress epidemic diseases of man and animals? has never been fully answered.

From 1857 on, the work of Pasteur and those who followed him turned bacteriology from a conjectural into a scientific discipline. The impact on medicine was immediate, and it was with few exceptions one sided. The pathologist analyzed the gross and microscopic changes in the cadaver and interpreted these end results of the infection. The study of the causative agents as living creatures, rather than the disease process itself, created the field of microbiology, a field already so broad that no single scientist can hope to deal with it competently. Experimental methods have brought bacteriology and pathology together. This left another area to be explored by the epidemiologist. Field investigations, clinical records, and laboratory researches on individual patients were correlated in an effort to understand the mass phenomenon of infection and disease

manifested in epidemics. The development of methods of investigating epidemics has made it possible to analyze newly discovered infections more efficaciously.

Initially, epidemiology was concerned with learning what maintained epidemic diseases. Medical bacteriology, fascinated by the rich rewards granted the unilateral search for new causes, at first failed to realize that infectious diseases are biological manifestations of parasitism. By placing the parasite in the foreground of the inquiry and by failing to consider as equally important the receptivity of the host to the parasite, the pioneers remained unaware of the full natural history of infection. Once it was recognized that most infectious diseases are characteristically asymptomatic, the strictly utilitarian concepts changed.

Today, the epidemiologist is less concerned with etiological specificity than with reactions between the infector and the infected. Study of the prime incitant of disease and tracing it to its natural environment share importance with appraisal of the spectrum-like individual, clinical, and immune variations within an infected group. Furthermore, the epidemiologist recognizes that knowledge of an infection in an individual patient is basic to comprehension of an epidemic. The broad field inquiries and experimental studies of the biology of infections indicate that the tragedy of individual events and the course of an epidemic are ultimately conditioned by innumerable variables in the constitution of the host and in the characteristics of the parasite. Study of both components of an infection must continue.

From this point of view, the contributions, even with respect to the parasite, which is more accessible to study than the host, seem modest. Bacteria and probably viruses are infinitely adaptable and versatile. Studies of bacteria and viruses have increased knowledge of their anatomy and physiology to the extent that the subject of bacterial heredity is topical. When it is argued whether bacteria have nuclei or reproduce sexually, difficulties arise about the precise use of these terms. This is not the place to enter into this controversy, but it can be said that bacteria contain material chemically akin to the constituents of the nuclei of plant or animal cells. This material is partitioned among the dividing bacterial cells, but, more important, identifiable components of one bacterium can be assimilated by another and transmitted to the descendants of that other, producing a race with a structure and properties different from those of the parent organism. These facts are in full harmony with what has long been known: Bacteria vary and mutate.

Successive generations of bacteria may differ fundamentally from those that preceded them, and the physical and chemical effects expressed as virulence produced by a bacterial population, even in a defined environment, cannot necessarily be predicted on the basis of previous experience. This fact may be irritating to the pure scientist who has studied bacterial chemistry. He does not know what to make of fugitive micro-organisms that differ from one another even when they originate from a single cell in a chemically defined medium. Allowing for variation, mutation, such sexual activities as transduction and transformation, and the appearance of a new generation every 20 to 30 minutes, change in infectious agents in so inconstant an environment as man and animals should surprise no one. But physicians and patients are bewildered about why epidemics wax and wane, and about why this person is stricken and his neighbor is not.

No one can say whether knowledge of present epidemics can be used to explain the ebb and flow of past epidemics. Changes in the state and circumstances of the host alone certainly cannot explain the great cyclic variations in virulence over the centuries. Mutation of the parasite as conceived in very general terms is, at least in the modern view, a decisive factor. Mutation of the parasite toward greater invasiveness and virulence along with favorable conditions in the host opens the way to rapid proliferation and transfer for a time. But as the host is reduced in number, the parasite tends to be subdued because its field of action is narrowed. Natural selection apparently acts in favor of a more balanced relationship in which host and parasite survive with minor damage to either. The epidemic explosive phase is relatively short; the stabilized endemic, symptomless phase, relatively long. This may or may not explain fluctua-

tions in epidemic patterns. Since infection is a natural phenomenon, infectious agents are likely to take new forms, and milder or deadlier infections may arise from the usual pathogenic agents or from nature's vast reservoir of feebly pathogenic or nonpathogenic creatures.

Infections do cross into regions where they were previously unknown, and they also may exist in unexplored areas. Man's entrance into uninhabited territories in quest of natural resources or land for agricultural development has led to the discovery of natural foci of zoonoses transmissible to man. These remain unrecognized until human beings come in contact with them. They constitute a potential danger, and their existence and localization should be anticipated.

How can a thoughtful student accept the view that the infectious diseases are losing their importance and that they will probably be conquered within a decade? Bacteriology and virology, with their important components microbiology and immunology, as cornerstones of epidemiology have made great contributions to medicine, public health, and preventive medicine. There are still challenges to the younger generation to apply effectively what is already known and in an adventurous spirit to decline acceptance of all prevailing views and incline to exploration of the remaining unknown. It has always yielded to determined, qualified investigators.

The laboratory worker observes that the number of specimens being received is growing and that the methods and the interpretation of results are becoming more complex. There is an unsatisfied need for diagnostic work and for the kind of assistance that can be furnished only by a qualified bacteriologist and epidemiologist receptive to problems in infectious diseases.

It seems appropriate on this occasion to discuss the natural history of two infections on which the predecessor of the National Institutes of Health—the Hygienic Laboratory—did pioneer work in the United States. My friendship with Dr. Dyer stimulated my continuation of plague studies during the past 15 years. Earlier counsel of Dr. George McCoy led the way. And without the studies on psittacosis in 1930 by McCoy, R. D. Lillie, H. E. Hasseltine, V. M. Hoge, and others, and the encouragement offered by the late Surgeon General Hugh S. Cumming, it is doubtful whether so extensive an effort would have been made to solve problems in California. In addition to the support given by the officers of the Public Health Service, perhaps sentimental ties with the country of my birth fostered my interest in these two infections. The cause of plague was first conclusively demonstrated by A. Yersin, a Swiss. Psittacosis was first described as a specific clinical entity by J. Ritter, another Swiss.

PLAGUE

Black Death claimed 14,000 inhabitants of the city of Basel between 1347 and 1353 and left its mark on many permanent records. Historical documents, religious ceremonies, and art treasures reminded later generations in that ancient city that plague was its worst visitation, surpassing war and famine in its impact. Family chronicles described the scourge and listed the medicaments that the head physician of the city hospital compounded by mixing 23 different herbs into what was called *aqua theriacalis*. This I well remember because translation of one of these documents from Latin into German was one of my assignments in the gymnasium in Basel.

At the time of that translation, the cause of plague had just been discovered, and the infection was embarking on its pandemic march out of Hong Kong. Perhaps nothing among the reminders left a greater imprint on my mind than a canvas by Boecklin, the famous Swiss painter, shown in the Basel gallery in 1897. Here the horrible feeling of the epidemic is conveyed by grotesque, triumphant Death, astride a monster, hurtling through a street.

While a graduate student at the Institute for Infectious Diseases in Bern, I assisted in the active immunization of horses with virulent plague bacilli. This experience provided ample opportunity to become acquainted with the plague cell and with procedures for guarding against infection. Efforts to develop a test on rats that would reveal the protective and, to a lesser degree, the curative properties of the

unpurified antiplague horse serum were disappointing.

Later, during a visit to Ann Arbor, Mich., Prof. F. G. Novy described the dramatic experiences in San Francisco in 1901, where he had been a member of an expert commission on plague. Subsequently, a worker in his laboratory had contracted pneumonic plague. From 1913 on, I followed eagerly the plague investigations conducted by the Public Health Service first in California and later throughout the 15 western States. Opportunities for studying plague developed slowly, but since 1920 the disease has been one of my main interests.

Epidemics in California

The urban murine phase of plague in San Francisco, with at least 159 cases and 77 deaths, terminated in 1908, and the subsequently discovered reservoir in wild rodents of rural areas yielded few specimens for study. In fact, by 1914 optimists contended that all discernible plague had been eradicated. But official records after 1915 continued to report that plague-infected squirrels were being found around the bay area. Human infections apparently did not occur, and for a time a feeling of security prevailed.

Then, like a thunderbolt, rapidly fatal pneumonic plague struck in Oakland, between August 15 and September 11, 1919. The circumstances of the outbreak, in which 13 persons died, including 2 physicians and 2 nurses, were described and interpreted by Force and Kelly (*1*). The first patient, who had secondary plague pneumonia after incision of a bubo in the right axilla, had hunted and shot squirrels in the Alameda foothills. The customary search for squirrels with gross anatomical lesions led to a small reservoir.

It was necessary then to look into the intrinsic and extrinsic factors that conditioned the episode.

With respect to the causative organism, this outbreak was compared with the earlier devastating epidemic of pneumonic plague in Manchuria. Because of the violence of both, it was thought that the plague bacillus involved differed from the ordinary strains, that it was specific, highly virulent, and pneumotropic. In both, lung lesions had been found in the responsible reservoir of wild rodents. It was believed that the respiratory infection was a mixed infection. Carefully planned experiments later showed the oneness of the plague bacillus, irrespective of host origin or symptoms. The strain isolated in the Oakland epidemic was not pneumotropic and differed neither biochemically nor serologically from the other continental strains.

Influenza interjected further diagnostic doubt. This disease had not entirely disappeared in August 1919, and the cause of death of one plague victim had been reported to be influenzal pneumonia. Methods of studying this virus had not then been developed, and the usual bacteriological tests on the lung specimen available did not answer the question.

The extrinsic factors in the Oakland outbreak had to be reconstructed from data collected after the epidemic. The temperature had been around 60° to 68° F. and the humidity low. Such climatic conditions would not favor the transfer of infected droplets carrying plague bacilli from one person to another, a fact suggesting that contact with the patients was probably close.

The climate was similar during October and November 1924 in another outbreak, this time in Los Angeles. There were 40 cases—29 pneumonic, 3 tonsillar, and 8 bubonic—and 35 deaths. Appearing in a few households, the infection was carried by visiting relatives or friends to other households, and these then became subsidiary centers for spread. An autopsy was performed in 9 of the 29 cases of pneumonic plague, and in 3 the evidence suggested contact infection through the oral or faucial mucosa. The significance of this type of infection was not known then. In 1926, Wu Lien-Teh reviewed 250 reported cases of pulmonary plague from various epidemics and mentioned tonsillar plague with primary cervical buboes in only 3 cases (*2*).

The epidemiology of the Los Angeles outbreak has never been critically analyzed, nor has an epidemiological report of it ever been published. On epidemiological grounds it is believed that secondary pulmonary invasion developing from bubonic plague of rat flea origin

started the epidemic. The recrudescence of rat plague in that area was a great surprise. Surveys begun in 1908, when an infected squirrel caused a human infection, and carried through until 1915 had revealed no infected rodents. Two possible sources of the infection in Los Angeles rats in 1924 were investigated: (*a*) infection in rats brought in from foreign ports through San Pedro, the port of Los Angeles, and (*b*) infection in ground squirrels in the area.

The first possibility was dismissed because plague-infected rats could not be located in the port. The second possibility seemed to fit the circumstances. The rats in that area did have contact with squirrels; infected squirrels were found in the urban section of the city; and squirrel fleas were found on the rats. The interchange of fleas between wild rodents and commensal rats had been recorded earlier (*3-5*) and has been observed since (*6*).

Wild Rodent Reservoirs

An ecologic study in 1946 on a ranch near Santa Paula, roughly 50 miles northwest of Los Angeles, established for the first time the simultaneous occurrence of plague in rats, ground squirrels, a cottontail rabbit, and their ectoparasites (*7*). One-fourth of the fleas taken from the rats were ground squirrel fleas carrying *Pasteurella pestis*. Plague was probably also transmitted from wild to commensal rodents in the rat epizootic in Tacoma, Wash., in 1942 and 1943.

Interestingly, rat plague has never been recorded inland in the western States. Not only are there fewer rats inland, but also there is no evidence that ectoparasites from other wild rodent reservoirs are transferred to the rat.

Recurrence of plague in commensal rats in countries where the principal natural reservoirs are squirrels and gerbils without notable repercussions in nearby human populations has not been adequately explained. The idea that commensal rats are the sole reservoir was based on observations that without exception domestic rats and the classic plague-bearing flea were abundant where bubonic plague was epidemic. Whether this combination is responsible for epidemics in India, Madagascar, Egypt, Senegal, Peru, Brazil, and elsewhere now requires thorough reevaluation.

As late as 1940, investigators familiar with plague in South America believed that natural infection of wild rodents was confined to Argentina. Then wild rodent foci were found in Venezuela, Bolivia, Peru, and Ecuador (*8*, *9*, and personal communications from Macchiavello). At first the investigators believed that the infection was not entrenched in smoldering wild rodent foci, but more recent observations indicate that it is.

In the brilliant investigation of the epidemiology of plague in Kurdistan Province in Iran, Baltazard and his associates discovered two pockets in which the reservoir included three species of sand rats (*10*). These rats were the most numerous rodents near the foci where there had been two explosive outbreaks of pneumonic plague. Since some of these rats were resistant to plague, they would not be likely to be wiped out by epizootics, but they could serve as reservoirs of enzootic plague. It is becoming apparent that the highly susceptible rodents, such as the marmot, the squirrel, and the rat, are not the permanent reservoirs of the plague bacillus. In his picturesque description, Baltazard states that if the rat has made the fortune of plague, it is not the original, probably not even the actual, proprietor of the disease, but only the disseminator.

It was once assumed that whenever a parasite brings about its host's death in a short time, the host is not the natural one or that it is a natural one in some unnatural environment. Now Baltazard's findings suggest that that concept may have to be modified: In Kurdistan some sand rats were quite resistant while others were highly susceptible to plague. Only analysis of the chromosomes, not of gross zoological characteristics, would permit the necessary distinction in susceptibility. As Baltazard has pointed out (in a personal communication), it now seems that maintenance of plague in focal areas requires resistant wild rodents capable of surviving the epizootics and thus of perpetuating the infection, as well as susceptible species capable of rekindling the infection. The ecologic factors in the focal habitual niches filled with hosts, parasites, and

vectors are obviously far more complex than they were once thought to be.

Influenced by the work of Baltazard, other workers have proceeded to find centers of wild rodent plague in Kenya, central Africa, and the United Provinces (Uttar Pradesh) in India. Heisch, while studying plague near Rongai in the Rift Valley of Kenya, found a focus in three different species of wild mice in a certain field (*11*). *P. pestis* was isolated from these rodents long after the widespread epizootic had died down and the animals in adjacent fields were proved by animal tests to be free from infection. After the field was ploughed up, infected rodents could no longer be found, but "permanent foci" persisted in the escarpments where rodent burrows were relatively undisturbed. The ecologically unstable plains are ideal for dissemination of *P. pestis* when conditions are suitable, but the infection retreats to the foothills between epizootics among the highly susceptible domestic rats.

According to studies supervised by Baltazard at the recommendation of the Expert Committee on Plague of the World Health Organization, the endemicity of plague in India is similar to that in Kurdistan, Kenya, and other parts of the world. It is due to an effective disease reservoir, not in rats, but in certain wild rodents, in particular in bandicoots (*Tatera indica*).

The geographic origin of plague has given rise to much speculation and much argument, and it has been hoped that bacteriology would eventually settle the issues. The glycerol reaction of a large collection of *P. pestis* strains has recently been restudied, and some interesting differences have been observed. The glycerol-positive strains, designated continental, are perpetuated in wild rodents in the old pestilence centers: southeast Russia, central Asia, Mongolia, Manchuria, Transbaikalia, and central Africa. The strains that apparently originated in the pandemic in Yunnan, China, in 1894 are glycerol negative and have been designated oceanic. These have been found in Kenya and in certain parts of the United States. One would expect the strains in the ports of Texas to be the pandemic glycerol-negative strains, but 3 of 29 strains isolated there from rats and 2 from patients were glycerol positive. Whether the glycerol reaction solves the nosographical problems is a question to be answered by further critical studies and interpretations.

Pathogenesis of the Infection

Nothing can happen in an epizootic or an epidemic that has not already been founded in a single infection. It is always important to understand the pathogenesis of bubonic, or zootic, and pulmonary, or demic, plague in experimental models, usually the mouse or the guinea pig. The pathogenesis of the infection after the introduction of *P. pestis* through the bite of a blocked infectious flea can be readily followed in these animals. It follows a standard pattern: afferent lymphatics to regional lymph nodes, to efferent lymphatics, to thoracic duct, to blood stream, to liver and spleen. When the bacteria multiply to such an extent that the liver and spleen can no longer filter them out, they appear again in the circulating blood. Active multiplication of *P. pestis* in the bloodstream, so essential to infection of the flea, is always terminal.

In this connection, the nature of septicemic plague should be clarified. As commonly defined, septicemic plague is a form of the disease in which, owing to the magnitude of the infection or to the low resistance of the host, the regional lymph nodes are overrun and the blood stream is immediately invaded. Because the infection is progressing so rapidly, the reactions taking place in the lymph nodes are overshadowed by the general condition of the patient or animal. What is considered primary septicemic plague is really bubonic plague in which the buboes are inconspicuous.

For these reasons it seems preferable to distinguish between two main types of human plague: the primary bubonic, or zootic, form and the primary pulmonary, or demic, form.

The spread of the infection in the immunized animal is similar to that in the unimmunized animal, differing from it only quantitatively. The organisms reach the bloodstream early, but they are destroyed so effectively that only isolation of the bacilli from the bone marrow testifies to the transient hematogenous spread.

The marked lung involvement regularly found in the absence of spleen or liver lesions in partly resistant or immune animals and in man dying after prolonged illness has not been satisfactorily explained.

This lacuna in our knowledge should be filled. Secondary lung involvement leads to cough and copious expectoration and often to pneumonic plague epidemics. Without knowing exactly what the mechanism is, one has to depend on epidemiological observations. Travelers who fall ill with bubonic plague before leaving an infected locality or en route therefrom are particularly prone to secondary lung involvement. Muscle efforts made by such people may cause detachment of infected thrombi from blood vessels around the buboes and may lead to lung embolism. Malnutrition and such extrinsic factors as cold and rainy weather may all contribute to impairment of resistance. Guinea pigs or squirrels surviving acute experimental plague for at least 6 to 10 days invariably have extensive secondary lung involvement.

At first it was believed that circulating toxin reduces the resistance of the lung tissue, just as staphylococcal toxin does (*12*). But guinea pigs and squirrels are quite resistant to the toxin. Mice and rats rarely have secondary pulmonary plague lesions. It is unlikely that the scattered foci of necrosis result solely from lowered resistance induced by toxin. Their location beneath the pleura suggests that they are initiated by bacterial emboli arrested in the arterioles and capillaries. In partially immune guinea pigs and naturally resistant ground squirrels, rapid mobilization of agglutinins favors embolus formation; agglutination promotes clumping of plague bacilli in the vascular beds. It is always striking that in the animals with secondary lung involvement the spleen and liver are singularly free from necrosis. Why neither the microphage nor the lymphoid-macrophage defense system is functioning effectively in the lung while it operates in the spleen and liver remains unanswered.

Discussion of secondary pulmonary plague recalls observations in the Los Angeles epidemics. Three plague infections described as tonsillar by experienced pathologists, Dr. George D. Maner and Dr. Lawrence Parsons, aroused no particular interest at the time because in the days of the Anglo-Indian Commission, in 1898 and 1899, it had been made clear that the plague bacillus can enter the host by channels other than the skin. An opportunity to investigate the portal of entry in tonsillar infection came quite accidentally.

Transmission of Pneumonic Plague

During studies on immunization of monkeys against pulmonary plague, healthy animals were exposed to cage mates with frank primary pneumonic plague in order to learn something about the contagiousness of the disease. A monkey (*Macaca mulatta*) infected by the intratracheal route and reacting with fever and definite roentgenologic evidence of pneumonia was placed in a cage with a healthy monkey. To learn whether *P. pestis* was being exhaled from the nasal passages of the infected animal, blood plates were held before its nose for ½ to 2 minutes at the time the healthy animal was put in the cage. In this interval, from 2 to 66 organisms were exhaled onto the plates. The healthy monkeys were left in the cages until the infected ones died: for from 2 to 72 hours. Of the 18 exposed, 9 contracted septicemic and 3 bubonic infection.

The procedure was then refined by confining the 2 monkeys in a large cage divided into 2 separate compartments by a coarse wire barrier. Bodily contact was thus eliminated, and a situation was created in which any exchange of *P. pestis* was through airborne droplets alone. Of the 8 exposed in this manner, 4 contracted septicemic infection.

Clinical and X-ray examinations and blood cultures demonstrated that primates exposed, with or without body contact, to cage mates suffering from primary pulmonary plague may contract plague and die. The rapidity of the course of the infection, the negative X-ray findings, and the early positive blood cultures in 13 of 16 successful transmissions left no doubt that the exposed animals died of "septicemic" plague. There was very little visible involvement of the lymph nodes. Systematic autopsies confirmed the clinical findings, but careful dissections invariably showed that the

superficial and deep cervical lymph nodes were slightly enlarged, hemorrhagic, and imbedded in edema. The lungs showed no consolidation; congestion and edema were at first glance interpreted as patches of pneumonia. Only 3 of the 26 exposed monkeys had pulmonary plague in the form of lobular foci extending to lobar involvement. Two of the animals with septicemic plague and no involvement of the lungs had ulcerations in the stomach and jejunum and buboes in the adjacent lymph nodes.

The gross anatomical lesions of the lymph nodes incriminated the upper part of the respiratory tract as the portal of entry of the plague bacillus, but generally there were no characteristic changes of the oral or faucial mucosa. Some congestion and swelling of the tonsillar region were noted in some animals. Examination of serial sections of the entire nasopharynx of six animals disclosed that the lymphatic tissues forming the ring of Waldeyer surrounding the oropharynx were the likely portal of entry of the organisms. Enormous masses of plague bacilli were embedded in the severely altered lymphoid tissue on one side, rarely on both sides, of the tonsillar sinus. The so-called tonsillar lymph nodes adjacent to the diseased lymphoid tissue invariably had the characteristics of primary plague buboes. As a rule, the palatine and faucial tonsils were not markedly involved. Clumps of plague bacilli were numerous and scattered through the epithelial layers of the pharynx. It is not unlikely that swallowing these clumps of bacilli led to the gastrointestinal lesions.

Two observations from these studies are of particular significance: Plague was transmitted through infectious droplets from primates with pulmonary plague; the apparent septicemic plague was bubonic tonsillar plague with cervical buboes. Most epidemiologists have believed that primary pulmonary plague is caused by an infection entering through the deeper portions of the respiratory tract, but a few, especially Kulescha (*13*), have considered the possibility that the organisms enter through the tonsils or other parts of the upper part of the respiratory tract and are then carried to the lungs by the blood stream. This idea was dismissed at one time with the statement that experimental observations did not support it.

Recent experiments by Druett and his associates (*14*) in which infection was introduced by means of bacterial clouds are most instructive. Two forms of plague, both originating in the respiratory tract of the guinea pig, developed, the form depending on the size of the particle conveying *P. pestis* to the host. Particles no larger than 1 micron initiated a bronchopneumonia that terminated in septicemia and death. Larger particles, 12 microns in diameter, deposited in the region of the head penetrated local epithelium and through the afferent lymphatics led to septicemia much earlier than occurs with organisms deposited on the bronchial or alveolar wall.

The monkeys infected by their sick cage mates suffered from the form of disease found in animals exposed to large-particle clouds, namely, septicemia arising from a primary focus of infection in the cervical lymph nodes with infarction, but no pneumonia. Attempts to establish an epizootic by cross-respiratory infection were abortive, probably because of the nature of the disease developing in the first cross infection.

Thus certain epidemiological observations are now partly clarified. What has been seen in man has been reproduced in animals.

Chemotherapy

The value of the antimicrobial drugs in treatment of plague has been soundly documented (*15*). In fact, one is justified in stating that it should be possible to cure any plague infection without complications if it is treated soon enough. Light and moderately severe bubonic plague infections have been cured in India with sulfathiazole, sulfadiazine, and sulfamerazine. The most spectacular effect of antiplague chemotherapy was that observed in Madagascar where pneumonic plague was treated with streptomycin, chloramphenicol, and tetracycline drugs (*16*). The overall curative effects were so impressive that failures in treatment, particularly in modern hospitals, were not anticipated.

A recent experience with a patient suffering from bubonic plague clearly teaches, however,

that there was still something to be learned. The patient had hunted in an area where a wild-rodent epizootic had been in progress. A plague pustule developed on his right ankle, and a corresponding inguinal bubo appeared. Other symptoms arose on the third day after exposure. He was then treated with penicillin, and the diagnosis was established and bacteriologically proved by lymph node puncture and blood culture on the fourth day after onset. Treatment consisted of administration of 2 gm. of streptomycin and dihydrostreptomycin, 2 gm. of terramycin, 4 gm. of sulfadiazine, and 600,000 units of penicillin every 24 hours. One week after onset, 3 days after specific treatment had been instituted, the patient died. The autopsy, conducted by two pathologists, one an expert in plague, proved all the tissues to be free from *P. pestis*; *Candida albicans* was present in the right and left lungs. Microscopic examination furnished evidence of activity of a potent toxin: edema of the myocardium, liver, and lungs, and nephrosis associated with hemorrhagic nephritis. It is well known, for instance, in diphtheria, that "serous inflammation" is entirely due to toxin of the causative organism.

The investigator of experimental plague is continuously impressed with the fact that the most effective drugs may kill the bacilli in the blood, liver, spleen, and bone marrow and reduce the number of viable bacilli in the focal lesions of the lymph nodes or lungs. Despite this remarkable therapeutic feat, however, the animals ultimately succumb, probably because of the damage done by the plague toxin (*15*). During the chemotherapy studies in Madagascar, a patient with pulmonary plague was not treated until the 48th hour of disease and died after 40 hours of therapy with chloramphenicol. At post mortem her tissues were free of *P. pestis*, and the death was ascribed to toxin.

Efforts to understand this intoxication and its treatment have been only partly rewarding. Potent antiserums containing antibodies against both infection and toxin have ameliorated this damage in mice, but not in monkeys. In more recent preliminary studies on mice with the *P. pestis* strain isolated from the California patient, streptomycin was indeed highly bactericidal; in fact, this strain was more rapidly lyzed by a combination of streptomycin and penicillin than was the control strain. When treatment with doses comparable to those used on the patient was begun late in the infection, animals died even though their tissues were completely free of *P. pestis*. That the deaths were probably attributable to the toxin was indicated by the observations that the effectiveness of the antimicrobial drugs was increased by from 15 to 50 percent when one dose of purely antitoxic serum was administered. This serum had a very high toxin-neutralization index and was completely devoid of demonstrable antibodies against infection.

Some of the basic knowledge essential to production of such an antiserum is available. Experiences in the United States with production of antiplague rabbit gamma globulin can readily be used to manufacture the amounts that might be required as an adjunct in treatment of the relatively few cases recognized in enzootic foci.

This leads back to some of the general thoughts expressed at the beginning of this lecture: Throwing great quantities of every drug against every infection without proper guidance by the laboratory will insure only the type of complications described here. As long as there are places where infections are spread to man, fundamental research in infectious diseases, efficient diagnostic services, and cooperation between the physician and the laboratory are essential to advances.

PSITTACOSIS

It once would have been said with confidence that the largest reservoir of psittacosis is the wild psittacine birds of the tropics: Australia, New Zealand, Mexico, and South America. But the list of wild birds in which the infection has been found has lengthened almost every time the virus is sought, and the continuing revelation of ornithosis in domestic poultry—pigeons, chickens, ducks, and turkeys—raises the question of its origin. Right now it is impossible to fit the fragments of information together. The answers cannot be found in sample serum surveys or virus isolation studies carried out in a single group of wild birds in a small area in a single season.

The stabilized association of birds with the basophilic elementary body psittacosis agent extends over such a wide geographic area and involves so many species of birds that it is hard to imagine that it has existed only as long as it has been known. Maintenance and transfer of the virus is assured by the flocking and nesting of birds. Fulmars, petrels, domestic and wild pigeons, chickens, ducks, and turkeys, birds that congregate and nest together, are hosts of viruses related to, but immunologically distinct from, the psittacine serotypes. The virus is rarely if ever found in species of more solitary habits. Under ordinary circumstances few birds die of the disease.

All observations on psittacine infections are consistent with the hypothesis that low-grade psittacosis has been enzootic for many years among Australian budgerigars, or shell parakeets, and among the more common wild South American and Australian parrots. Psittacosis was undoubtedly imported with the original breeding stock first into England and then into nearly every country of the world. The enzootic infection in parakeets bred in Europe and America in all probability derives from the natural infection of the Australian budgerigar from which these parakeets are descended. However, this does not necessarily mean that the virus did not exist elsewhere in the world at that time.

Course of the Infection in Birds

The course of the infection in the wild bird population has not been studied extensively. This focus has rarely given rise to known human infections; man does not ordinarily associate with wild birds closely enough to endanger his health. It is necessary to resort to analogy to describe what may be the natural course. Under stress of egg laying and hatching, the hen with latent infection excretes virus through the alimentary canal. Susceptible nestlings contract the infection; most of them recover and some become carriers. It seems likely, too, that the virus goes through periodic phases of increased virulence, and if an adequate number of birds is susceptible, an epizootic may result. The uncertainties of an outdoor climate may contribute to spread of the infection. This leaves unexplained the occurrence of the infection in widely separated areas in birds that do not migrate. It may be found eventually that the virus is not so exotic or so tropical as it once seemed.

It is not surprising that the best known segment of the natural history of psittacosis is the infection in an unnatural niche: the parakeet-breeding aviary. When the parakeet is bred and raised in captivity in large numbers under conditions that differ radically from those of the Australian bush, the host-parasite relationship undergoes some changes. The parasite itself apparently behaves differently. The virus strains isolated from acutely infected cage birds have been distinctly more virulent than most isolates from acutely infected Australian parakeets. Occasionally, epizootics have killed 5 to 10 percent, sometimes an even higher proportion, of flocks in aviaries or pet shops.

During the acute infection the organism abounds in the diarrheal droppings and nasal secretions, and through these the parasite is conveyed to young birds. Some latently infected hens under stress of egg laying and hatching have excreted the virus more frequently and possibly in higher concentration than have latently infected hens not under this stress. Birds less than 6 months old are then the likely victims of the disease. The greater susceptibility of immature parakeets under experimental conditions and in aviaries is conclusively proved. The outcome of the infection in some maturing birds is asymptomatic infection grossly evident only in an enlarged infected spleen. This enlargement probably indicates that the parakeets have been infected but have suppressed or completely eliminated the infector. The latent infection rates have ranged from 5 to 80 percent in aviaries and pet shops.

Factors in Resistance

Resistance is an important factor in the natural history of psittacosis, and most of what is known of it has been learned through experimental studies and observations on the course of the infection in aviaries. Here again no single factor can be given credit; heredity, age, and previous infection all participate.

Certain birds have an innate resistance to

psittacosis and do not become infected. The proportion of naturally immune birds varies from flock to flock. It may be low, for example, in parakeet-breeding flocks that are being inbred for certain feather coloring.

Age seems to condition resistance to some extent. Liability to fatal infection declines with age, but susceptibility remains fairly constant. Highly toxic isolates induce symptoms in only a few adult parakeets; less toxic ones induce only transient symptoms or latent infection. Within 30 days about 25 percent of infected adult birds have eliminated the invading parasite from their tissues.

In the early days, when symptomatic disease was the only criterion of infection, it was thought that parakeets that had been experimentally infected and had then recovered had a strong immunity to infection. This is supported by the apparent immunity of a large proportion of the adult population of aviaries in endemic areas. It is further supported by the high susceptibility of flocks that have been successfully kept infection free and by the resistance of treated birds a month after artificial infection. Accidental introduction of infected birds into aviaries, cages, or zoological gardens may be followed by fatal, but more frequently by latent, infections. How long the resistance manifested in a small group of treated birds would persist one cannot say. Infection unquestionably does provoke immunity; there is a specific acquired antigen-antibody immunity. It is the duration of the immunity that varies from bird to bird.

And the effectiveness of any of these factors varies according to the vigor of the infector.

Control Methods

When latent infection becomes epizootic in an aviary, usually some departure from good husbandry and cage hygiene has taken place. Formerly, only destruction of diseased birds brought the epizootics under control. A great deal can be said in favor of attempting to control the disease, despite its infrequent occurrence in man, and with the knowledge available it should be possible to eliminate the infection from aviary breeding stock. Until this major undertaking can be achieved, the proper handling of shipments and distribution of birds in the retail trade would reduce and possibly eliminate some major sources of human psittacosis. Chemotherapy will serve as one of the most effective instruments.

That drugs inhibit multiplication of large viruses of the psittacosis-lymphogranuloma venereum group was first demonstrated with the lymphogranuloma venereum virus and the sulfonamides (*17*). Not all strains are equally sensitive, and it is the exceptional strain of the psittacosis agent that is susceptible. Aureomycin and terramycin are effective against the psittacosis virus because they prevent initial-body formation and almost completely inhibit growth, but they do not destroy the virus. Since 1950 the curative effect of these antibiotic drugs has been well established.

If adequate amounts of the drugs are given for an adequate time, at least 10 days, the mortality rate is less than 1 percent. If the disease is not treated, the rate is 20 to 40 percent. The lifesaving ability of the tetracycline drugs is spectacular in comparison with that of penicillin (*18*). The difference can be readily explained. Penicillin arrests cell division, but the organisms continue to grow and abnormally large forms develop (*19, 20*). The effect of the tetracycline compounds is more profound, for it includes inhibition of growth.

In large-scale field trials acute infections have been suppressed within 4 to 8 days, and 98 to 100 percent of latent infections have been cured with daily doses of 1.0 to 1.5 mg. of oxytetracycline, chlortetracycline, or tetracycline (a total of 15 to 30 mg. per bird). Intramuscular administration of the antimicrobial drugs is laborious and, if carried out on infected birds, exposes the injector to the risk of infection. The successful impregnation of hulled millet, sunflower seeds, or peanuts with tetracycline now allows administration of the drug in a uniformly acceptable and stable feed. This method is the most convenient way of suppressing the reservoir of human infections.

It must be remembered, however, that birds free from infection are still susceptible. Offspring from an aviary stock free from psittacosis are highly susceptible to acute psittacosis, and the infection, of course, may become latent. Treated flocks and their offspring must be pro-

tected against infection by chemotherapy whenever exposure is suspected. A program aiming at the distribution of psittacosis-free birds, readily identifiable by characteristic leg bands, may be achieved if the bird-breeding and bird-distributing groups cooperate wholeheartedly.

The Disease in Nonpsittacine Birds

With respect to psittacosis arising from nonpsittacine birds, epidemiological histories invariably report that the patient handled sick or visibly diseased carcasses of birds or was exposed to a flock that at the time of exposure or shortly before contained sick birds. The pathogenicity and virulence of the strains isolated from pigeons, chickens, and ducks and from the patients who have contracted the infection from them have been low for mammals and highly susceptible avian species. Most infections caused by these strains are inapparent. Despite the extent of the avian reservoir, the human infections are mild and infrequent. Few of numerous attempts to convert these distinct serotypes into more virulent strains by repeated passage through mice or ricebirds have been successful.

In pigeon lofts and poultry yards exchange of the parasite is similar to that in parakeet aviaries, but the balance is disturbed in favor of the parasite less frequently than it is among crowded cage birds in aviaries. It has occurred in young birds and in flocks that have been inadequately fed, poorly housed, or crowded (*21*).

Now a new ecologic problem has arisen. Infections among poultry workers and rendering plant employees comprise 398 (nearly a fourth) of the 1,687 human psittacosis cases reported in the United States in the past 5 years. These have been due to exposure to anatomically diseased poultry, principally turkeys. Enough isolations have now been made from diseased and apparently healthy turkeys raised in different parts of the United States to warrant consideration of the ecology of this phase.

Certain virus isolates from the fibrin-coated air sacs, peritoneal lining, pericardium, and blood of turkeys that had succumbed to natural infection have been exceptionally virulent for mice and guinea pigs. Sometimes they have induced fatal infection within 48 hours, and when injected intravenously in the high dilution of 1:1,000, they have formed a highly potent toxin that kills white mice. Only 2 virus isolations have been made in the 398 human cases. These were identical to the turkey strains in their intense virulence. In outbreaks in Texas, New Jersey, and Oregon highly virulent isolates from the viscera of poultry have been identical to those isolated from these two plant workers in Texas and Oregon.

Random examination of spleens of apparently healthy turkeys not involved in human outbreaks in Texas, California, and Michigan have yielded seven isolates belonging to the psittacosis group. On primary isolation they were of low virulence for mice and guinea pigs. Two became virulent after repeated mouse passage, and in dilutions not exceeding 10^{-5} they fatally infected mice. However, they retained their low toxicity and did not fatally infect guinea pigs. Despite numerous passages the remaining five isolates retained their low virulence for mammals.

Several isolates were derived from a flock of turkeys in California in which mortality had not been undue. When the first part of the flock was processed, the hearts and livers of some birds were condemned because they were visibly diseased. The remainder of the flock was serologically tested, and 83.5 percent were positive. Of 88 employees who had handled the diseased poultry, the serums of 3 gave complement fixation reactions indicative of previous exposure to agents of the psittacosis group. None of the employees gave a history of illness. The serums of residents and employees on the turkey ranch where the infected flock was raised did not react in the complement fixation test.

This single observation does not justify the conclusion that the turkey ornithosis serotypes of low mammalian virulence are equally harmless to man.

Results of indirect complement fixation tests indicate that many flocks have been infected, but since the infections were mainly latent little is known of them. At this preliminary stage of the inquiries, it seems that natural infection of low virulence in turkeys resembles that in Australian parakeets and some pigeon flocks.

The gross anatomical lesions observed in the processing of the flock of subclinically infected birds mentioned above suggest that this strain was more virulent than the usual strains of low virulence.

There has been little opportunity to study the natural history of ornithosis in the turkey flocks responsible for the explosive outbreaks of human illness in processing plants. In only a few instances is there opportunity to follow the course of epizootics. The epidemiologist encounters the end result of the epizootic on the processing line. Naturally, he speculates on possible sources of infection.

Since the droppings of the acutely diseased birds contain the parasite in abundance, it is no surprise to find 50 to 80 percent of a flock are seropositive within a few weeks. However, while knowledge of the pathogenesis and course of the infection in the turkey is still so sketchy, one has few leads to what initiates and promotes the epizootic. The parasite may be introduced into the flock by wild birds, by other turkeys, through eggs, contaminated feed, or biologics, or even by visitors to the ranch. For incubator-hatched and artificially brooded poultry, the nest infection chain does not exist. Ecologic investigations such as those made in the parakeet-breeding establishments must be undertaken and extended over several years before the natural history of the disease in turkeys will be understood.

Ornithosis in turkeys is of growing interest to large groups: consumers, flock owners, poultry industries, agricultural agencies, poultry processors, labor unions, insurance companies, health agencies, and biologists. Each component has something to gain if methods of control can be worked out. If control were to be approached by all concerned in an investigative and determined spirit, it seems credible that something could be done. No one can predict at this time how serious the problem may become.

Summary

The age of the biological phenomenon of parasitism is at least that of recorded history. For centuries, man's survival has been chaotically interferred with by the infectious diseases, in pandemic form dramatically. In the last half century, man, through his intelligence and diligence, has begun to control this chaos effectively for the first time. The host's reaction against certain parasites is being fortified by immunization, and the life of certain parasites is being destroyed by antimicrobial drugs. These advances are good cause for great rejoicing. They are not cause for believing that parasitism holds no further challenge to man's ingenuity.

Very few parasites depend solely on man for their survival. Even if all the people of the world could be immunized, it would be an oversight of the characteristics of biological processes to hope that the infection concerned would thereby be banished from the earth. Immunization, which in some infections protects even the eagerly susceptible, usually must be repeated in the individual and certainly with each new generation. Effective chemotherapy must wait until the host is manifestly affected adversely by the parasite. Both of these defenses, magnificent but temporary, leave the parasite free to carry on its usual latent existence untouched: to multiply, to adapt, and to exert its capricious effects on the host.

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Johns Hopkins University to Revise Medical Curriculum

A revised program of medical education, which will reduce the period of study and emphasize the humanities, is scheduled to begin at the Johns Hopkins University School of Medicine in the fall of 1959. The plan cuts 2 years from the training period for a carefully selected group of students and shortens the course for others by 1 year.

A total of $10 million was granted by the Public Health Service, the Ford Foundation, the Rockefeller Foundation, the Commonwealth Fund, and by other private sources for the construction of a new basic science building and for additional faculty.

Program objectives are to shorten formal medical education without sacrifice of quality; to overcome the barrier between the liberal arts and the medical sciences; and to encourage students to follow careers in the basic medical sciences, such as physiology, anatomy, and pharmacology, in which there is the greatest shortage of teachers and research workers.

Candidates with adequate "motivation and maturity" who have completed 2 years of college will be permitted to enter medical school, where they will pursue a 5-year course. During the first 3 years of medical school, they will continue studies in the liberal arts, at the end of which they will receive the bachelor of arts degree.

Students accepted after 3 or 4 years of college will begin medical school with the second year of the 5-year program.

For all students the last year of medical school will be combined with the first year of internship at the Johns Hopkins Hospital. In addition to 24-hour responsibility for patients, the student will have a 2-month elective period for work in the basic sciences or further clinical training in any of the hospital departments.

Although the years of medical training are reduced, with a consequent cut in medical education costs, the actual period of training is shortened relatively little. The academic year is increased from the present 32 weeks to 40 weeks; the fifth year covers 50 weeks.

The Manchester Variety Of Shigella flexneri 6 Isolated in Kentucky

D. J. Schliessmann, M.S., W. T. Cooley, M.S., and Robert Rabin, Sc.D.

THE Manchester variety of *Shigella flexneri* 6 has been found to be prevalent among the normal population of preschool children in the coal mining region of eastern Kentucky. In diarrheal disease studies conducted by the Cumberland Field Station of the Public Health Service's Communicable Disease Center, this strain was isolated one or more times from 69 children during a 20-month period.

To our knowledge, no previous reports of the identification of the Manchester variety in the United States have appeared in the literature, although several investigators advise us that the strain has been isolated in this country. W. H. Ewing of the International Shigella Center in Atlanta, Ga., has confirmed the identification of this strain, which was isolated by L. F. Ey and C. C. Croft of the Ohio Department of Health during a disease outbreak in Mansfield, Ohio, in July 1949. In this outbreak, 9 infants died and 172 of the estimated 468 residents in an area of substandard homes gave a history of being ill. Ewing has said also that the Manchester variety has been isolated in Louisiana, and W. W. Ferguson of the Michigan Department of Health has reported identification of the strain in his State.

Mr. Schliessmann is chief of the Cumberland Field Station, Communicable Disease Center, Public Health Service, West Prestonsburg, Ky. Mr. Cooley is currently in charge of laboratory services of the Berea College Hospital, Berea, Ky., and Dr. Rabin is currently with Smith, Kline, and French in Philadelphia.

Dr. W. H. Ewing of the International Shigella Center, Atlanta, Ga., confirmed the identification of 98 Shigella flexneri 6 isolations (5 Manchester and 3 Boyd 88) and 22 other Shigella isolations reported in this paper.

The Manchester variety is one of three presently known biotypes of *S. flexneri* 6. In 1925 Clayton and Warren isolated the first biotype from the feces of a girl suffering from diarrhea in Newcastle, England (*1*). Later, these workers obtained similar organisms during a small epidemic of diarrhea in a children's home (*2*). The mannitol negative, aerogenic bacillus described by them, subsequently named the Newcastle dysentery bacillus, was serologically related to other *S. flexneri* serotypes. Hardy and others (*3*) have reported that the Newcastle variety is the cause of acute diarrheal disease in England, India, Africa, and South America.

In 1933 Downie, Wade, and Young (*4*) described organisms which they isolated from five diarrheal cases near Manchester, England, and from a mild case of dysentery in a Nigerian laboratory worker. These organisms were serologically identical with the Newcastle bacillus, but differed biochemically in their ability to ferment mannitol aerogenically. They became known as the Manchester variety of *S. flexneri* 6.

A third biotype, which has been designated the Boyd 88 strain, was first reported from India by Boyd (*5, 6*). The organisms he described were aerogenic, fermented mannitol, and were serologically identical to the Newcastle dysentery bacillus. The pathogenicity and recovery of the Boyd 88 biotype have been reported throughout the world.

Scott (*7*) has shown that the bacilli of Boyd 88, Manchester, and Newcastle are all serologically identical.

Material and Method

One phase of the diarrheal disease studies in the coal mining region of eastern Kentucky is the collection each month of rectal swab specimens from normal preschool children in selected mining camps and rural populations. Specimens are obtained at the homes in the manner described by Hardy and Watt (*8*), by inserting a sterile cotton swab into the rectum. Immediately after withdrawal from the rectum the swab is used to streak a *Shigella-Salmonella* (Difco) agar plate and is then placed in a tube of tetrathionate broth. The

inoculated plates are subsequently incubated at 37° C. in the laboratory, and typical colonies are picked to triple sugar iron (TSI) agar at 24 and 48 hours. The swab in tetrathionate broth is incubated at 37° C. for 24 hours and then streaked on brilliant green agar plates, which are then incubated. Colonies typical of *Salmonella* are picked to TSI agar at 24 and 48 hours. Biochemical and serologic examinations of organisms suspected of being *Shigella* or *Salmonella* are performed as described by Edwards and Ewing (*9*).

Results

During a 20-month period, September 1954 through April 1956, *Shigella* organisms were isolated from 272, or 3.3 percent, of 8,392 specimens obtained from normal preschool children. As shown in the tabulation below, the most prevalent type encountered was *S. flexneri* 6, which represented 43 percent of all *Shigella* isolations. Of the 118 *S. flexneri* 6 isolations, 95 percent were Manchester and 5 percent were Boyd 88 biotypes. *Shigella sonnei*, representing 22 percent of the total *Shigella* isolations, was the second most prevalent type. Seasonal peaks in *Shigella* isolations occurred in the fall and early spring, with the proportion of the Manchester variety to all other shigellae remaining fairly constant.

	Number of isolations
S. dysenteriae 2	7
S. flexneri 1b	24
S. flexneri 2a	26
S. flexneri 3	5
S. flexneri 4a	33
S. flexneri 6, Manchester variety	112
S. flexneri 6, Boyd 88 variety	6
S. sonnei	59
Total	272

The 112 positive isolations of the Manchester biotype were obtained from 69 children in 52 families. The organism was isolated once from 48 children, twice from 14 children, 3 times from 1 child, 4 times from 1 child, 5 times from 4 children, and 9 times from 1 child. In 12 children the organism was recovered in 2 consecutive months, and in 2 it was recovered for 3 and 6 successive months respectively. In seven children the bacillus was recovered twice with a negative culture during the intervening month. From 4 children a second recovery occurred after 2 negative monthly cultures, and from 1 child a second isolation was obtained after 3 successive negative cultures.

Discussion

In view of the few reports of the occurrence of the Manchester biotype in the United States, the high prevalence of the organism in normal populations in Kentucky is striking. The findings may be of particular significance to epidemiological and laboratory workers. It is possible, of course, that the situation in these somewhat isolated communities is not duplicated elsewhere, but it is also possible that the organism is actually more widespread in this country than the paucity of reports would indicate.

Biochemical reactions of the Manchester bacillus are atypical in comparison with the reactions of the other shigellae in that they ferment glucose and mannitol with the production of gas. The Manchester biotypes encountered were nonmotile and did not utilize citrate, produce indol, or hydrolize urea. Lactose, adonitol, and salicin fermentations were negative. The organism consistently fermented glucose and mannitol, with production of gas in both carbohydrates. Glucose fermentation is of particular significance to diagnostic laboratory workers since reactions in TSI agar have been used as one of the principal biochemical screening tests in enteric bacteriology. Gas is formed by the Manchester bacillus in TSI and Kliger's agar slants in small to moderate amounts frequently sufficient to rupture the media. Therefore, cultures showing an alkaline slant and acid butt with gas should not only be considered as possible "paracolons" or non-H_2S-producing salmonellae, but also should be checked as this biotype of *S. flexneri* 6. The Boyd 88, the Manchester, and the Newcastle biotypes cannot be differentiated by serologic tests with absorbed antiserums since they are serologically identical. Final identification and differentiation of the biotype is dependent upon both biochemical reactions and slide agglutination with absorbed antiserums.

Of the 21 children in this study with more than one infection, approximately one-half were members of families in which their preschool siblings became infected, thereby providing ample opportunity for intrafamilial reinfection. For example, M. C. and E. C. are 2- and 9-year-old sister and brother. M. C. was Manchester positive on specimens taken in July, November, and December 1955, and again in March and April 1956. E. C. was positive in August, September, and October 1955, and again in February and March 1956. Since the Manchester bacillus was found only once in 70 percent of the children infected and since there was ample opportunity for reinfection in children having infections for consecutive months, the duration of infection presumably averaged about 1 month. This period is consistent with previous observations by Watt and his coworkers (*10*) on the duration of the carrier state for the *S. flexneri* group.

Summary

Two biotypes of *Shigella flexneri* 6 have been isolated from normal preschool children in eastern Kentucky. Of 272 *Shigella* isolations obtained from specimens taken September 1954 through April 1956, 112 (41 percent) were Manchester bacillus and 6 (2 percent) were the Boyd 88 variety.

Attention is called to the atypical biochemical reactions of the Manchester bacillus in comparison with other *Shigella* and to the possibility that this biotype is more widespread in this country than is currently believed.

The average duration of the carrier state appears to be approximately 1 month, which is comparable to duration of infection of other *S. flexneri* types.

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detection of hearing loss in preschool children

MARGARET L. GEYER, M.S., and ALFRED YANKAUER, M.D., M.P.H.

AN INDIVIDUAL pure tone sweep check has proved relatively effective in mass screening preschool children for hearing loss in a study in Rochester, N. Y. A great majority of the children were screened successfully, and threshold tests confirmed hearing loss in about half the screening failures. The screening test, an adaptation of the sound toy test described by Myklebust (*1*), requires a minimum of equipment and time.

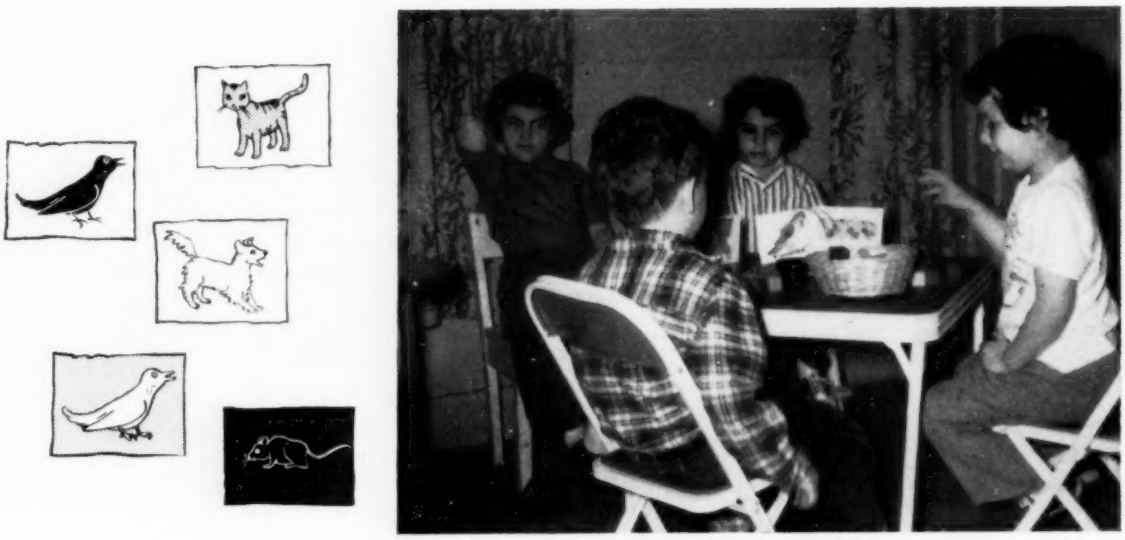
The advantages of finding cases of hearing loss in preschool children have long been recognized. Speech training is most effective if begun before the child is of school age; progress of the hearing loss may be arrested by early treatment; and school adjustment is facilitated by knowledge of the child's capabilities on admission to school. However, mass testing of preschool children has not been generally undertaken, primarily because of doubt whether it could be done efficiently. Although a wide variety of methods for testing hearing of young children has been devised, none has been generally accepted as completely satisfactory for mass screening.

Because of the wide variation in procedures recommended for testing hearing in preschool children, the Rochester study was designed with a twofold purpose: (*a*) to work out a simple but effective hearing test for mass screening of an apparently well preschool population using readily available equipment and (*b*) to judge the value of mass screening with the test from the standpoint of case finding and time required to carry on the program.

Material and Method

Children in the study were drawn from those attending guided observation play groups or parent cooperative nursery groups housed in 10 public schools, those enrolled in 3 private

Miss Geyer, an audiologist, has been with the Rochester Board of Education, Rochester, N. Y., since 1945. Dr. Yankauer, at one time deputy health commissioner of Rochester, has been director of the bureau of maternal and child health, New York State Department of Health, Albany, since 1952.



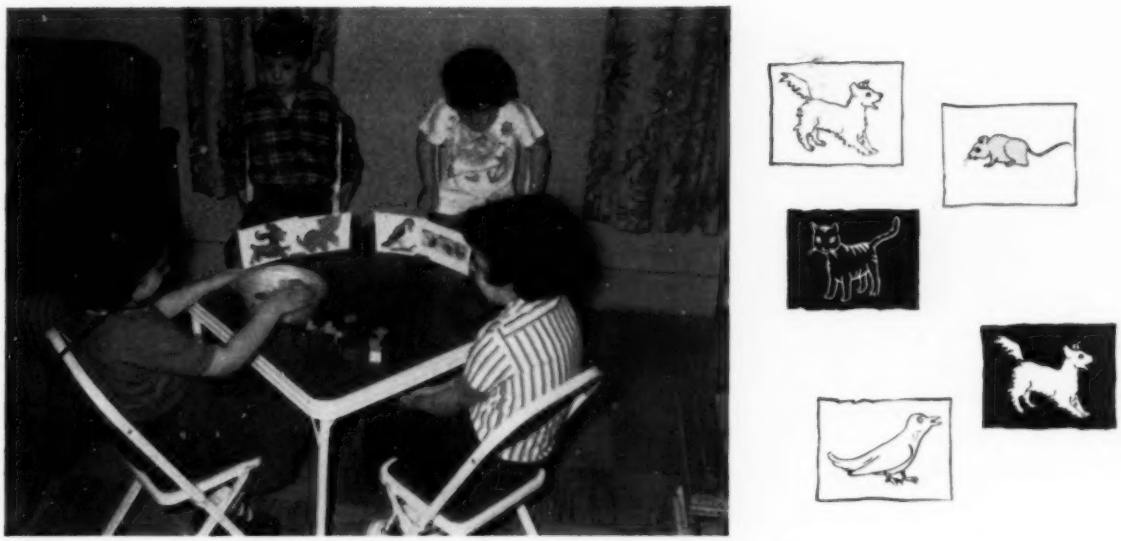
Practicing for the pure tone test, the child drops blocks into the basket.

day nurseries, and a group registering for kindergarten for the next year in 1 public school.

Screening was done in a quiet room in a school. An audiometer (*A*) with binaural headphones was used on the first 2 days of screening, but because some of the children resisted wearing the double headphones, an instrument (*B*) with a single headphone attached to a metal headband was used for all subsequent screening tests. A square of sponge rubber to which a picture of a bird had been pasted was used to cushion the free end of the headband. The single headphone was not only more acceptable to the children, but it also facilitated communication with them during the screening. The frequencies used were 1,024, 2,048, 4,096, and 512 c.p.s., presented in that order. Testing was limited to four frequencies because the short attention span of young children makes it necessary for the tester to work quickly. The frequencies selected were used by Myklebust (*1*) in a research study with preschool children and were the basis for the percentage table prepared by Fowler and Sabine for the American Medical Association in 1947 (*2*).

A child-size folding table with a red leather top and two matching folding chairs were used. Two children were seated at the table, and two more children were seated nearby so that they could observe. As recommended by Mykelbust (*1*), pictures of a dog, a cat, a bird, and a mouse were used to represent 512, 1,024, 2,048, and 4,096 c.p.s. respectively. The pictures were mounted on 4″ x 6″ white cards, and the cards were inserted in slits in small wooden blocks so that the pictures were upright and in the children's view. In front of each of the two seated children was a pile of 1-inch solid-colored wooden cubes. A small basket was placed on the table so that the children could reach it with ease. It should be noted that the equipment needed to supplement standard audiometer equipment is inexpensive and easy to obtain.

To prepare the two children at the table for the test, the audiometer earphone was placed face upwards on the table so they could hear the tones when they were turned on at full intensity. It was explained to the children that they would hear the sound of a dog, a cat, a bird, and a mouse, the tester pointing in turn to each picture, and that when they heard the sound they were to drop a block into the basket. The tones were sounded, at irregular intervals, until the two children were conditioned, that is, until the children gave clear evidence by their response that they knew precisely what to do whenever they heard a tone. This conditioning procedure was repeated with each set of two children. When screening 3- and 4-year-olds the tester placed the phone on her own head in an effort to ward off timidity or resistance on the child's part. After a moment



Animal pictures represent the four tones used in the screening test.

she removed it, and an assistant placed it on the child's right ear, the tester saying to a boy that he was to be an airplane pilot and to a girl that she was to be a telephone operator. In addition to placing the earphone on the child's ear, the assistant saw that the child always had a sufficient number of blocks before him and helped him to and from the testing room. Use of a testing team of two made it possible to work with more dispatch.

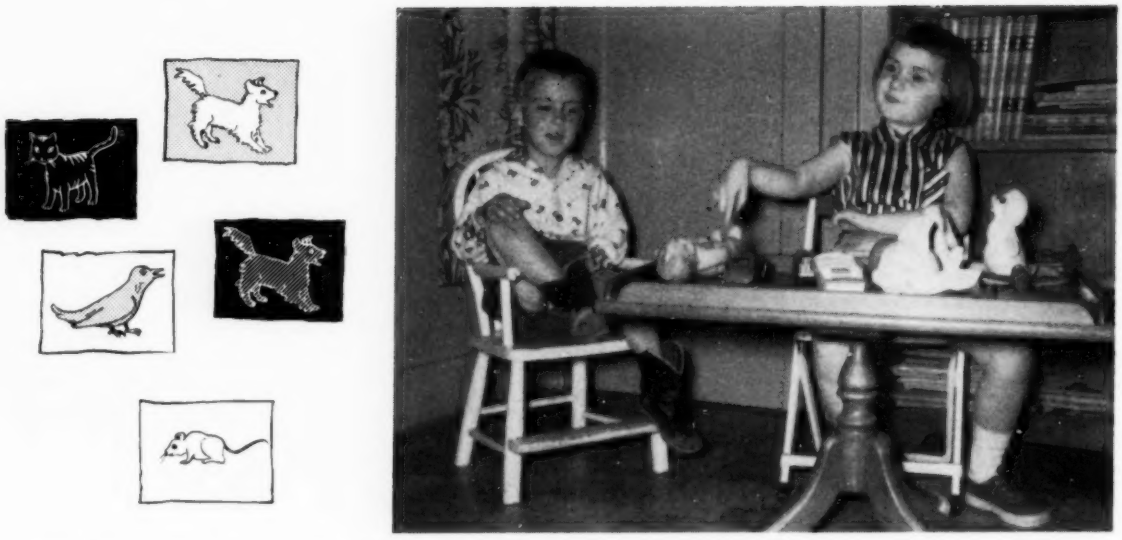
The tester swept through the four frequencies, presenting them in the order given above to one child at a time at an intensity of 20 db. Each time the child heard a tone he would drop a block into the basket, which was now directly in front of him. Each frequency was presented twice. If the child indicated he heard the tone both times, he was considered to have passed at that frequency; if he failed to hear both times, he was considered to have failed. If he heard the tone only once out of the two presentations, it was presented a third time, and he passed or failed at the frequency presented depending upon his reaction to the third presentation. If the child failed to hear any one frequency in either ear he was considered to have failed the screening test.

The interrupter switch on the audiometer was used between each presentation of each tone, at irregular intervals, so that the tester could immediately detect random responses. If the child dropped a block into the basket when no tone was sounded, he was cautioned to listen carefully and to drop the block only when he heard the tone.

For each child who failed the screening test, an appointment was made for a more complete evaluation at the clinic of the Rochester Hearing and Speech Society. This consisted of a second screening test, followed by a pure tone threshold test and an otological examination for all children who failed the second screening test. In addition, all children who reported for the clinic evaluation, regardless of the outcome of the second screening test, were given a free field speech reception test.

An audiometer (*C*) with binaural earphones was used for pure tone threshold testing. Auxiliary equipment and general procedure were the same as described for the screening test. Frequencies of 1,000, 2,000, 4,000 and 500 c.p.s. were presented in that order, the method described in the Manual for a School Hearing Conservation Program (*3*). A child who had a loss of 20 db for any two frequencies or a loss of 30 db for any single frequency was considered to have failed the threshold test (*4*).

The free field speech reception test was the children's auditory test developed by Monsees (*5*). This test uses a phonograph recording of nine words familiar to young children: baby, duck, car, dog, bus, fish, airplane, boat, and ball, each word being preceded by the carrier phrase, "Show me the." The child was



For the speech reception test, the child points to an object when he hears it named.

seated at a table 3 feet from the loudspeaker. On the table were toys representing the above-named objects. In a practice session with live voice, the procedure was explained to the child. The phonograph recording was then played at a level about 30 db above the child's pure tone threshold. Speech reception threshold was determined by attenuating to a level where the child could point correctly to the toys 50 percent of the time.

The otological examination consisted of inspection of nasal passages, pharynx, and tympanic membrane.

Medical recommendations were made by the otologist of the Rochester Health Bureau, Dr. Lawrence J. Nacey. Educational recommendations were the joint decision of the otologist, a consultant in speech and hearing therapy of the Rochester Board of Education, Dr. Rolland J. Van Hattum, and the tester. All screening and threshold testing were done by Geyer.

Results

A total of 461 children ranging in age from 2½ through 5½ years were given the initial screening test. The test appeared to be beyond the ability of 8 children (1.7 percent) who were suspected of being mentally retarded, and 22 children (4.8 percent) could not be tested because of shyness, fear, or negativism. The percentage of children who could not be screened varied from 12.3 percent at age 2½–3½ to 3.3 percent at age 4½–5½ (table 1).

Fifty-three of the 431 children (12.3 percent) successfully tested failed the initial screening. All but three of these failures were given the second screening test. Twenty-eight children failed the second screening test, and all 28 (6.5 percent of the total group followed) also failed the threshold test. No significant relationship between test failure and age of child is apparent (table 2).

All the children whose hearing was within normal limits at 500, 1,000, and 2,000 c.p.s. in one or both ears on the second screening or

Table 1. Unsuccessful sweep check testing, by age

Age	Total children in study	Screening unsuccessful	
		Number	Percent
2 yr. 6 mo.–3 yr. 5 mo.	65	8	12.3
3 yr. 6 mo.–4 yr. 5 mo.	213	16	7.5
4 yr. 6 mo.–5 yr. 5 mo.	183	6	3.3
Total	461	[1] 30	6.5

[1] Includes 8 children with possible mental retardation and 22 children whose cooperation could not be elicited.

Table 2. Results of screening 428 [1] preschool children, by age

Age	Number of children screened	Failed first screening test		Failed second screening and threshold tests	
		Number	Percent	Number	Percent
2 yr. 6 mo.–3 yr. 5 mo.	56	9	16.0	5	8.9
3 yr. 6 mo.–4 yr. 5 mo.	195	19	9.7	7	3.6
4 yr. 6 mo.–5 yr. 5 mo.	177	22	12.4	16	9.0
Total	428	50	11.7	28	6.5

[1] Does not include 3 children who failed first screening test but who were not given subsequent tests.

the pure tone threshold test (according to the above-mentioned standard) obtained a speech reception threshold equal to or 5 db lower than that obtained by first- and second-grade children with normal hearing on whom the system was calibrated. However, whereas the latter performed the test until it was completed, the children in our study, especially the 3- and 4-year-olds, sometimes lost interest and had to be recalled to the task. For children with bilateral loss on the pure tone threshold test, the binaural average was determined. The difference between the speech reception threshold and the best binaural average of the pure tone threshold varied from 2 db to 15 db, with a mean of 11 db. In general, it was felt the two thresholds were in close enough agreement to confirm each other.

Medical care was recommended for 19 of the 28 children who failed the pure tone threshold test. Speech reading was recommended for 1 other child and considered as a future possibility after reevaluation for 3, 2 of whom also had medical recommendations. Thus specific medical or educational recommendations, or both, were made for 21 children, 5 percent of the total group followed.

According to a record of the time it took to condition and screen each child, the average time per child was 5½ minutes.

Discussion

The findings of this small study indicate that mass screening of preschool children is a worthwhile public health procedure. Of 431 apparently well children, 6.5 percent were found to have a valid hearing loss, and medical or educational recommendations for treatment were made for most of these. The screening test proved successful with the vast majority of the children, and it was a fairly accurate case finder with a relatively low rate of overselection.

It should be emphasized, however, that it is one thing to screen preschool children but quite another to obtain an accurate threshold test on them. While both procedures require patience, testing experience, understanding of young children, and keen observation on the tester's part, the former can be performed quickly and is simply a matter of the child's indicating whether or not he hears the tone. Obtaining a true threshold of hearing (not of interest) for each frequency poses a real problem. Myklebust (*1*) has pointed out the improvement in response as the child grows older. For example, he found that the mean threshold reading at 1,000 c.p.s. for children between 3 and 3½ years (6 ears) was 14.16 db, in comparison with 3.50 db for children between 5 and 5½ years (10 ears). This point has been brought out also by Westlake (*6*): "Children of 3 and 4 years of age show less consistency in their response to the pure tone tests and show a wider deviation from accepted normal thresholds than the older ones do, but these are very probably due to other factors than auditory acuity."

A final point to be made in discussing hearing screening programs, particularly when they involve very young children, is the significance of the child's response or inability to respond to the hearing test itself. Lack of response is a revealing symptom of the child's total behavior, and if persistent it should be followed up by more complete audiologic and neuropsychiatric evaluation in a diagnostic center. Since many retarded children have central auditory perceptive problems, accounting for inability to respond to a screening test on the basis of mental retardation is not justified.

With these points in mind, it would seem realistic to recommend that careful mass screening be carried on with preschool children and that two successive failures to pass the screening test should be followed up by a pure tone threshold test. Referral to an otologist should be made on the basis of the threshold audiogram even though its complete accuracy may be questioned by the tester. The growth of nursery schools and organized play groups for children of preschool age should provide an accessible population for such a public health program.

Summary

In a study in Rochester, N. Y., an individual sweep check for hearing loss was successfully administered to all but 6.5 percent of 461 children from 2½ through 5½ years of age. Fifty of fifty-three children who failed the screening test were screened a second time. Twenty-eight of these children failed the second screening test and a subsequent pure tone threshold test. Thus 6.5 percent of 431 children successfully screened were considered to have a hearing loss. Medical or educational recommendations were made for 21 of them.

The average time required to condition and screen a child in this study was 5½ minutes.

From the standpoint of prevention, amelioration, and educational therapy, mass screening of the preschool population is worth while. The method described here appears to be one way of effectively and quickly screening this population.

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(*B*) Western Electric, model 6 BP, Audivox, Inc., Boston, Mass.

(*C*) Peters, model 23, Alfred Peters & Son, Ltd. Electron Works, 89 Arundel Street, Sheffield, England (distributed in this country by Sonotone Corp., Elmsford, N. Y.).

DOCUMENTATION NOTE

A bibliography of 25 articles on testing of hearing in young children has been deposited as document No. 5289 with the American Documentation Institute, Photoduplication Service, Library of Congress, Washington 25, D. C. A photoprint copy may be obtained by remitting $1.25; a 35-mm. microfilm copy by remitting $1.25. Advance payment is required. Make check or money orders payable to Chief, Photoduplication Service, Library of Congress.

Pesticide Residues in Fluid Market Milk

PAUL A. CLIFFORD

DURING the fall of 1955, each of the 16 Food and Drug Districts submitted at least 100 samples of market milk to the Division of Antibiotics, Food and Drug Administration, Washington, D. C., where they were checked for residual antibiotics (*1*). In addition, 800 of these samples, 50 from each district, were analyzed by the Division of Food for pesticide residues.

Surveys in 1948, 1949, and 1951 had shown that traces of DDT could be found in about 25 percent of market milk samples. A fairly specific but somewhat long procedure, the Schechter-Haller method (*2–4*), was then available for detecting DDT, but more recently many other pesticides have come into use, and residues of lindane, technical BHC, methoxychlor, Rhothane, heptachlor, toxaphene, chlordane, members of the aldrin group, Perthane, Dilan, Lethane, and others might be encountered in milk. For most of these no specific test method exists. In addition to the group of chlorinated organics, trace residues of the organic phosphate pesticides, such as parathion, and Systox, might be found. A further complication was recognized from the start: Little is known about the metabolism of most of these products; some or all might degrade to unknown products of unknown toxicity.

Because of the dearth of specific methods, and because the application singly of the available ones to hundreds of samples would involve more work than a limited staff could handle, a bioassay "sort-out" test was applied. E. P. Laug of the Division of Pharmacology has perfected a bioassay with flies and applied it to the determination of DDT, lindane, endrin, and other pesticides (*5–7*). When only one toxicant is known to be present, the results can be made remarkably quantitative. When the toxicant is unknown, or a mixture of toxicants is present, fly mortality gives a positive indication of their presence and, barring synergistic effects, at least some idea of the amount. Thus, the fly bioassay appeared to be well suited to routine sort-out work.

The Division of Pharmacology collaborated in this survey by running the fly bioassays on the prepared extracts of the milk samples. There were 801 samples in all. The Schechter-Haller method was later applied to a number of samples which tested strongly positive by bioassay, and paper chromatographic techniques were applied to these latter samples in order to identify the residues that caused mortality to flies (*8*).

Experimental Studies

All the chlorinated organic pesticides are fat-soluble and if present can be presumed to occur in the fat component of the milk. Sample preparation must thus involve the separation of trace quantities of the various pesticides from a relatively great quantity of butterfat. The fly bioassay cannot be applied directly to extracted butterfat; extraneous oily residues of more than about 20 milligrams will suffocate the flies. Further, there is a limit to the sensi-

Mr. Clifford is chief, Methods Research Branch, Division of Food, Food and Drug Administration, Department of Health, Education, and Welfare. Participating in the survey were the following FDA chemists: Paul A. Mills, William O. Winkler, J. William Cook, Alfred K. Klein, Lloyd C. Mitchell, Nancy Pugh, C. Richard Tamorria, John F. Tighe, Edwin P. Laug, and Frieda Kunze.

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tivity of the bioassay; as the test is conducted the flies will not react to, for example, much less than 5 micrograms of DDT. This amount of DDT would represent 0.05 p.p.m. for a 100-gram sample, and previous experience had shown us that amounts of this order were to be expected in some milk. Accordingly, it was necessary to develop techniques capable of separating microgram quantities of the various pesticides from 4 to 5 grams of butterfat. Good paper chromatograms likewise require that oily residues in the milk extracts be negligible.

Fly Bioassay

One-day-old flies from a special strain were employed. They were DDT-susceptible flies originally supplied by the Entomology Research Division of the Agricultural Research Service, U. S. Department of Agriculture, and maintained in the FDA Division of Pharmacology for about 10 years. Details of the bioassay may be summarized briefly: 1.30 gm. of flies (90 to 100 individuals), anesthetized with CO_2, were placed in flasks containing the milk residues plus 5.0 mg. oleic acid matrix and kept there overnight. A standard series, for example, 5, 8, 12.5, and 20 μg. p,p′ DDT plus 5.0 mg. oleic acid, and at least one blank flask containing only oleic acid, were also run (*5–7*). The percentage of mortality in all flasks was determined next morning.

It should be emphasized that mortality can be caused by factors other than the presence of pesticides; excessive fatty or waxy residues, while nontoxic in themselves, will suffocate the flies. Fortunately, flies exhibit a characteristic reaction to chlorinated pesticides, a well-defined dancing or jittering. In our experience, this characteristic symptom has as much, if not more, diagnostic value as the number of killed flies. The test was considered negative when the symptom was not observed.

In a number of samples, with no dancing or jittering, mortality was in excess of 10 percent. To avoid false positives such samples were reported as "negative, but excessive kill." It is possible that residual pesticides contributed to the high mortality and that characteristic toxic symptoms were missed during the overnight exposure periods.

Had only DDT been present, the mortality of the flies in the DDT standard flasks would have provided a means of assay. In this work, a "positive" indicated the presence of one or more unknown toxicants and, of course, some idea of the amount present. We had a few 100 percent kills. All positive fats were reserved for further work.

Chromatography

Paper chromatograms were run on the 160 milk fats, about 10 from each district, which exhibited the highest toxicity to flies. The general technique was that of Mitchell (*8*). Considerable preliminary work was necessary to determine the conditions under which all of the pesticides likely to occur in milk would separate on the chromatograms. Various solvent systems in varying proportions were tried: methanol-water, dioxane-water, acetone-water, and methyl Cellosolve-water. This latter system was finally selected, as it would separate DDT, which showed 2 spots for the 2 isomers of the technical product; DDE, the ethylenic decomposition product of DDT; DDD, or Rhothane; methoxychlor; lindane, or gamma BHC; technical BHC, which gave 2 spots, one due to the gamma isomer; and members of the aldrin group. Chromatographic separation of other pesticides—chlordane, toxaphene, heptachlor, Dilan, Perthane, and Lethane—was also investigated.

Schechter-Haller Method

One hundred sixty-nine of the milk fats exhibiting the highest fly kill, selected on the basis of about 10 from each district, were run by the Schechter-Haller colorimetric method. This method is not entirely specific for DDT; DDD, or Rhothane, the dichloro analog of DDT, interferes, as will Dilan to some extent. As the method is applied, methoxychlor and Perthane do not interfere, but various degradation products of DDT cause interfering colors (orange or pink). Technical DDT also contains about 25 percent of the o,p′ isomer which yields an orange color instead of the distinctive purple of the predominant p,p′ isomer. Thus, the test is only roughly quantitative; it was used mainly to confirm the chromatographic results. Actually, the colors produced ranged from a nor-

mal purple to intermediate pinkish "off-shades." However, as they were due to DDT or related compounds, any one of these colors was called positive.

Organic Phosphate Pesticides

Each of the 801 samples was checked for organic phosphate pesticide residues by an in vitro cholinesterase inhibition test. Here again preliminary testing of methods by means of recovery runs with various organic phosphate pesticides was necessary. For the test, portions of the $CHCl_3$ extracts of the milk were brominated. This converts most thiono and dithio forms of phosphate pesticides to potent inhibitors. Extracts were then tested for inhibition by a ferric hydroxamate colorimetric method which measures residual acetylcholine (*9*, *10*).

Results

On a countrywide basis the fly bioassay applied here revealed that 62 percent of the 801 milk samples contained pesticide residues (table 1). Most of the residues were in trace amounts that were not identified specifically. Thirty-eight percent of the samples were called negative; 11 percent of the total number caused fly kills in excess of 10 percent but were classed as negative because characteristic toxic effects were not observed.

In the chromatographic results from 160 samples, DDT, DDE, BHC, lindane, DDD, and methoxychlor were identified in the milk chromatograms (table 2). It was not unusual to find as many as 4 of these in 1 milk sample. Members of the aldrin group were not encountered; nor were chlordane, toxaphene, and heptachlor. Technical chlordane and toxaphene are complex mixtures and both chromatograph as streaks instead of spots. It is possible that very small amounts of these or their metabolites may have escaped detection because the attenuated streak might not have registered on the chromatogram. DDA, a known metabolite of DDT, was likewise not found in the milk samples. The repeated occurrence of DDD may be somewhat surprising, but we are certain that the identification was positive. It may occur per se or as an impurity in technical DDT. It has not been mentioned as a metabolite of DDT.

Usually the chromatograms were clear cut

Table 1. Results of fly bioassay on milk samples, Food and Drug Administration survey, 1955

Food and Drug District	Number of samples	Positive [1]		Negative [2]		Negative, but excessive kill [3]	
		Number	Percent	Number	Percent	Number	Percent
Atlanta	50	24	48	26	52	8	16
Baltimore	51	29	57	22	43	5	10
Boston	48	27	56	21	44	10	21
Buffalo	50	24	48	26	52	5	10
Chicago	52	30	58	22	42	7	14
Cincinnati	50	28	56	22	44	6	12
Denver	50	29	58	21	42	4	8
Kansas City	50	29	58	21	42	3	6
Los Angeles	50	37	74	13	26	6	12
Minneapolis	50	27	54	23	46	5	10
New Orleans	50	43	86	7	14	5	10
New York	50	31	62	19	38	9	18
Philadelphia	50	28	56	22	44	13	26
San Francisco	50	41	82	9	18	0	0
Seattle	50	37	74	13	26	2	4
St. Louis	50	32	64	18	36	1	2
Total	801	496	[4] 62	305	[4] 38	89	[4] 11

[1] Test called positive, regardless of mortality, if flies showed toxic symptoms.
[2] No toxic symptoms observed.
[3] No toxic symptoms, but kill greater than 10 percent.
[4] Average.

and easy to read; occasionally extraneous residues either streaked the chromatogram or produced diffused, fluorescent spots which, however, were distinct from the typical dark spots of silver formed by the chlorinated pesticides or their derivatives. An unidentified silver spot of low R_f value occurred in a large proportion of the samples, and a similarly unidentified spot of high R_f was occasionally noted.

An effort was made to concentrate the materials responsible for these two unknown spots and to check them for toxicity. A number of samples which gave both the high and low spots were composited and spotted on paper; after development the proper sections of the paper were leached and the residues exposed to flies. There was no detectable toxicity.

The ethylenic derivative of p,p′ DDT, or DDE, was often noted in the chromatograms. Possibly it occurs in milk as a metabolite of DDT, but it could have resulted from the breakdown of DDT during storage and during the analytical process. In fact, possible decomposition of pesticides during transport and storage of the samples was one of our major worries; slight acidities caused by souring of the milk samples, or the development of free acids in the stored fats, could destroy pesticides of the aldrin group. Possibly this is the reason these were not encountered.

In the 160 high mortality samples selected out of the 801 total, pesticides were found in the following order of incidence: BHC, 60 percent; DDT, 54 percent; lindane, 26 percent; DDD, or Rhothane, 24 percent; methoxychlor, 3 percent; DDE, either a breakdown product or metabolite of DDT, 36 percent. Usually the DDE spot occurred in conjunction with DDT, but occasionally it occurred alone.

About 53 percent of the high mortality samples, 89 out of 169, gave positive Schechter-Haller colors ranging from faint pink to deep purple (table 3). Read as p,p′ DDT (600 mμ), results ranged from a high figure of 1.46 p.p.m. on the basis of the original milk down to traces (about 3 μg per 100-gm. sample or 0.03 p.p.m.). The high figure is not accurate for DDT because DDD was also detected on the chromatogram of this sample.

In practically every case the colorimetric and chromatographic results were in at least qualitative agreement; sometimes the chromatogram registered a faint DDT spot for samples which gave no perceptible Schechter-Haller color.

In the early stages of the work we encountered two samples of milk which seemed to

Table 2. Chromatographic results on milk samples exhibiting the highest toxicity to flies, Food and Drug Administration survey, 1955

Food and Drug District	Number of samples	Number of samples containing:					
		DDT	DDD	DDE	BHC	Lindane	Methoxychlor
Atlanta	8	7	3	0	7	1	0
Baltimore	11	6	4	3	4	3	2
Boston	10	5	1	3	6	0	2
Buffalo	6	3	3	2	5	1	0
Chicago	10	4	0	3	4	6	0
Cincinnati	11	1	2	1	7	2	0
Denver	10	8	1	5	5	5	0
Kansas City	13	4	2	5	4	5	1
Los Angeles	10	10	9	9	4	2	0
Minneapolis	10	2	0	4	8	2	0
New Orleans	11	7	1	5	7	2	0
New York	10	1	0	2	6	4	0
Philadelphia	10	2	1	1	2	8	0
San Francisco	11	11	10	11	10	0	0
Seattle	10	10	2	2	10	0	0
St. Louis	9	5	0	1	7	1	0
Total	160	86	39	57	96	42	5
Percent of total		53.8	24.4	35.6	60.0	26.3	3.1

Table 3. Schechter-Haller test[1] on samples exhibiting the highest toxicity to flies, Food and Drug Administration survey of milk, 1955

Food and Drug District	Number of samples	Number positive	Percent positive	Range as DDT (p.p.m.)
Atlanta	11	7	64	trace–1.46
Baltimore	11	7	64	traces
Boston	11	6	55	traces
Buffalo	10	3	30	traces
Chicago	10	6	60	trace–0.16
Cincinnati	10	3	30	traces
Denver	10	8	80	trace–0.10
Kansas City	13	10	77	trace–0.32
Los Angeles	11	10	91	trace–1.20
Minneapolis	11	6	55	trace–0.04
New Orleans	10	2	20	traces
New York	10	3	30	traces
Philadelphia	10	1	10	0.06
San Francisco	11	11	100	trace–0.29
Seattle	10	4	40	trace–0.08
St. Louis	10	2	20	traces
Total	169	89	53	trace–1.46

[1] Reveals DDT and its decomposition products or metabolites, or both. DDD and Dilan are partial interferences.

NOTE: Trace represents approximately 3 μg. per 100-gm. sample or 0.03 p.p.m.

yield some anticholinesterase activity; however, as the work progressed to its conclusion, no more positives were found. Because of this, and especially in the light of more recent research on milk, these two seemingly positive results are now questioned. It seems unlikely that organic phosphate pesticide residues occur as such in present-day market milk.

Summary

1. More than 60 percent of 801 market milk samples collected in a countrywide survey in the fall of 1955 contained residues of chlorinated organic pesticides as indicated by the fly bioassay procedure used. Most of the residues were in trace amounts that were not identified specifically. The samples showing the highest kill of flies, about 21 percent of the samples, were examined by paper chromatography and by the Schechter-Haller method for DDT and related compounds.

2. One or more of the following, BHC, DDT, lindane, DDD (Rhothane), methoxychlor, and DDE, have been identified by paper chromatography in some of the residues.

3. Market milk may contain up to 1.5 p.p.m. DDT or related compounds or both. Results by chemical methods, such as the Schechter-Haller colorimetric method must be accepted with caution unless interferences are known to be absent.

4. Two obvious sources of contamination of milk with chloro-organic pesticides are residues on forage and contamination as a result of insecticide sprays either on the cows themselves or in the barns and dairies. It is not known which of these is mainly responsible for the contamination. Work designed to settle this point is now in progress in the Food and Drug Administration.

5. Organic phosphate pesticide residues were not detected in these milk samples by an in vitro cholinesterase inhibition test.

(A limited followup survey conducted during the winter of 1956–57 by Atlanta, New Orleans, Los Angeles, and San Francisco districts revealed little or no contamination of market milk with either BHC or DDT.)

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Details of the methods used in preparing the samples and subjecting them to bioassay and analysis will be supplied by the Food and Drug Administration upon request.

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Seventh International Cancer Congress

The Seventh International Cancer Congress, sponsored by the International Union Against Cancer, is scheduled for July 6–12, 1958, in London, England. Scientists and physicians are invited to submit previously unpublished or unreported papers on experimental or clinical aspects of cancer, or on cancer control. The deadline for registering without payment of late fee and for submitting papers is January 1, 1958.

A preliminary program and applications for registration and submission of papers may be obtained from either the Secretary General, Seventh International Cancer Congress, 45 Lincoln's Inn Fields, London, W.C. 2, England; or Dr. Harold F. Dorn, Secretary General, International Union Against Cancer, National Institutes of Health, Public Health Service, Bethesda 14, Md.

Travel allotments of about $530 each are available to a limited number of scientists and physicians residing in the United States to cover air tourist fares on a special 15-day overseas round trip; a 6-day per diem allowance; and reimbursement for registration fee. Investigators invited to take part in one of the symposiums before or after the congress may apply for additional funds.

Applications for travel allotments should be in the form of letters in sextuplet giving age, training, titles of publications in cancer or related fields, academic or professional title, and institutional affiliation. The letters should be countersigned by the department director or administrative officer. Applicants for travel allotments submitting papers to the congress must include 6 copies of an abstract not exceeding 250 words of each paper; those not planning to present papers should include 6 copies of a major, current investigative work. The letters and abstracts must be submitted before January 1, 1958, to the Chairman, USA National Committee on the International Union Against Cancer, 2101 Constitution Avenue, NW., Washington 25, D. C.

Applications for assistance toward travel expenses are entirely separate from applications for registration for the congress and for the submission of papers to the program committee. All applicants will be responsible for their own passports, visas, registration, travel arrangements, and hotel reservations.

1956 Summary of Disease Outbreaks

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THE PATTERN of disease outbreaks in 1956, especially those which were waterborne or foodborne, did not differ materially from that of the previous 5 years. About the same proportion of waterborne and foodborne outbreaks occurred in schools, public eating places, and private homes. Likewise, many of the underlying causes, namely, poor food-handling practices, were mentioned as frequently in the reports for 1956 as in former years.

An examination of the reports of epidemiological investigations of disease outbreaks of all types during the year suggests that a considerable number were conducted with a minimum amount of effort on the part of the investigator. At the other extreme, some reports indicated that unusual occurrences of disease were investigated with meticulous attention to pertinent details.

Some investigations falling into the first category were limited in scope because the epidemic was brought to the attention of health authorities so late that a satisfactory report could not be made. Other outbreaks may have received scant attention because they were not considered to be important, and still others perhaps because trained personnel were not available for conducting investigations.

On the other hand, as there are each year, a number of reports of investigations were outstanding, although not all were concerned with diseases or illnesses of great public health importance. For instance, one widespread outbreak of typhoid fever was investigated and reported in great detail, and the probable source of infection was determined. Other examples include a large number of human cases of psittacosis, occurring in one State, which were associated with turkeys; a foodborne outbreak of gastroenteritis in a high school; an outbreak of shigellosis traced to a water supply; and a number of investigations of single cases of a disease, including plague and suspected smallpox. Many of the investigations were conducted by teams of specialized personnel from local, State, Federal, and, occasionally, nongovernmental agencies. The various types of skills found in such teams might include those of medical officers, microbiologists, veterinarians, sanitary engineers, or entomologists. When the talents of such persons are brought to bear on a disease outbreak problem, it is probable that the underlying as well as the immediate causes will be brought to light.

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Waterborne Disease Outbreaks

There was an increase in the number of waterborne disease outbreaks in 1956 compared with those of the past several years. In 1955, there were only two outbreaks with an unknown number of cases, probably less than 50. However, in 1956, there were 9 waterborne outbreaks of disease in which 1,719 persons were affected.

The 1956 outbreaks represent 2 rather large and 2 small outbreaks among persons who drank water from contaminated public systems. One outbreak involving about 800 persons was classified as shigellosis. *Shigella flexneri* was isolated from stool specimens from several of the patients. The specific organism was not found in the water, but an organism resembling shigella was isolated. There was

substantial evidence that the city supply had been contaminated with raw water from a mountain stream. Evidence of fecal contamination was found along the stream, probably deposited there by campers known to have used the area. In another outbreak, about 700 persons in a small town became ill after the public water supply became heavily contaminated with surface drainage following a sudden rain storm. A third outbreak occurred in one section of a city. Here, the supply was contaminated by raw water from a stream being forced into the public water system by a sprinkler system pump of a resident living in the area of contamination. The fourth outbreak was traced to contamination of the water system during repair of a city main. When a ditch was opened about the main it filled with water from seepage, necessitating continuous pumping while the repair was being done. Although the line was flushed upon completion of the work, no sterilizing agent was used.

Three other outbreaks of gastroenteritis occurred in camps where untreated water was being used. In one camp, the local water company pumped raw creek water into the system because a well, ordinarily used as a source of supply, produced insufficient water during periods of peak demand. The remaining outbreaks were in two separate families whose water supply was private. In one family, *Salmonella typhimurium* was isolated from stool specimens, and the water in an old dug well was found to be contaminated. The outbreak in the other family resulted from poison being dumped into a well.

Three other disease outbreaks were reported in which water was suspected, but definite evidence was lacking. One was hepatitis (number of cases unknown) in a school. Another was among social workers at a gathering held in a place where new water pipes had been installed. It was reported that the pipes had not been flushed when the system was placed in operation. The third occurred in persons attending a church camp and is described under typhoid fever.

Milkborne Disease Outbreaks

The number of milkborne disease outbreaks also exceeded the number reported in 1955. This is because 27 outbreaks of staphylococcal food poisoning involving more than 700 persons resulted from the ingestion of milk reconstituted from dry milk. Most of these outbreaks occurred among school children who drank United States surplus dry milk furnished through the school lunch program. No outbreak in 1956 was associated with pasteurized milk. Four cases of brucellosis occurred in a rural family who used raw milk from infected cows. Among customers of a restaurant, 80 persons became ill after eating a cheese sauce. Although none of the sauce was available for bacteriological examination, there was sufficient epidemiological evidence to incriminate it. The ingredients offered a rich media for pathogenic organisms, and the product was left at room temperature for 4 or 5 hours. The source of infection in two other outbreaks was traced to ice cream served at family gatherings, one of which was a picnic. In one outbreak, *S. typhimurium* was isolated both from the ice cream and from stool specimens of the patients. No source for either of these outbreaks was found. The second outbreak was believed to have been milkborne. Raw milk used in ice cream was considered to be the vehicle of infection. This, however, was not proved.

Other Foodborne Disease Outbreaks

The number (210) of foodborne outbreaks other than milk and milk products reported in 1956 is a little more than the 193 in 1955 but less than the 234 in 1954. This amount of variation suggests that no significant changes have occurred in incidence of these foodborne diseases in the past 3 years.

Most of the outbreaks were staphylococcal food poisoning, followed closely by unspecified types of gastroenteritis. A few miscellaneous organisms, including paracolon bacilli and streptococci, were found during the investigations of some outbreaks. Most of the outbreaks of typhoid fever and shigellosis, and almost half of the salmonellosis outbreaks were traced to carriers of the respective organisms who had handled or prepared food. Illness or infection was found in food handlers in a few of the outbreaks of staphylococcal food

poisoning and unspecified gastroenteritis. The sources of most of these outbreaks were not determined, but inadequate refrigeration was commonly a contributing factor permitting incubation of pathogenic organisms in food items.

As in previous years, poultry meat was most often incriminated in the outbreaks. Turkeys accounted for a large proportion and chickens for only a fraction of the total outbreaks. Beef, ham, and pastries were mentioned in almost equal numbers, about the same as in previous years. Potato salad was mentioned in only a few outbreaks but showed almost a fivefold rise over the number for the previous year, when outbreaks attributed to this item reached a low ebb.

Typhoid Fever

During 1956, there was an increase in numbers of cases of typhoid fever reported in the United States. Part of this increase was due to a relatively large number of cases which occurred early in the year in the North Central States. The fact that many of the cases were caused by one phage type (E_1) and that they were scattered over several States suggested that some article of food widely distributed through commercial channels might be the vehicle of infection. However, after an intensive investigation by State and Federal agencies, no common source of infection could be found. This widespread occurrence is not included in table 2.

Another group of persons became infected at one place but became ill in and were reported from several States. However, all of them are included in tables 1 and 2 as an epidemic originating in one State. Following a church camp meeting attended by several hundred people, 27 persons became ill after returning home. Epidemiological evidence indicated that water from a well at the camp site was the medium of spread. Furthermore, an epidemic of mild diarrhea which occurred during the camp meeting strengthened the belief that this supply of water was responsible for spread of the typhoid infection. It was determined that a typhoid carrier had attended the camp and the organism isolated from her was the same type (C_2) as that isolated from the majority of the cases of typhoid fever.

Six other outbreaks consisting of only a few cases each were reported, all of them in association with carriers. Three were traced to contaminated food, and one was probably waterborne. A number of single cases for which epidemiological reports were received are not included in table 2.

Salmonellosis

Most of the 23 outbreaks of salmonellosis reported in 1956 were attributed to food, but in 6 outbreaks the vehicle of infection was not determined. Of the foodborne outbreaks, 4 were associated with turkeys, 1 with chickens, and 1 with ice cream. One outbreak of salmonellosis was waterborne.

Nine of the outbreaks were traced to carriers. In one outbreak, 521 persons in a mental institution became ill over a 10-day period. A food handler was found to be a carrier of *Salmonella newport*, but two organisms, *S. newport* and *S. typhimurium*, were isolated from stool specimens of cases traced to this source. Two other outbreaks were reported among persons patronizing establishments selling products to the public. In one of these, prepackaged chicken salad was the vehicle. A total of 323 cases were reported in connection with this outbreak, but the total number was estimated to be at least 3,000 symptomless infections in approximately 100,000 persons who were exposed to 28,000 individual cartons of chicken salad distributed over a 4-week period. Of 18 food handlers who had some contact with this salad, 5 were found to be carriers of *Salmonella blockley*. The second outbreak affected persons who ingested cream-filled cookies from a bakery that distributed this product in several western States. Of the remaining outbreaks, 5 were in universities and schools, 1 in a country club, 1 followed a community gathering, and several smaller outbreaks were in restaurants, labor camps, a farm, a bakery, and a club.

Two outbreaks of salmonellosis occurred in hospital nurseries for the newborn. *Salmonella oranienburg* was isolated in one such out-

break, and the same organism was isolated from a woman in the isolation unit. However, there was no contact between the nursery and the isolation unit except through medical officers and nursing supervisors. The source of this outbreak was not found. The source of the other outbreak was a mother whose stool yielded the same organism as that found in the infants.

Organisms isolated from specimens collected during the investigation of the *Salmonella* outbreaks were *anatum*, *blockley*, *chester*, *enteritidis*, *heidelberg*, *infantitis*, *montevideo*, *meunschen*, *newport*, *oranienburg*, *rabislaw*, *thompson*, and *typhimurium*.

Shigellosis

Of the 8 outbreaks of shigellosis reported, 1 was waterborne, 2 were transmitted by person-to-person contact, and 3 were traced to carriers handling food. In two, the source and mode of infection was not determined.

One of the outbreaks spread by personal contact was in a farm labor camp. Here, poor environmental conditions and lack of adequate water supply were contributing factors. The other was in an elementary school where there was evidence of poor personal hygiene which might allow rapid transmission of the disease by the fecal-oral route. Examination of the restroom facilities at this school revealed that water pressure was low and insufficient to flush toilets during periods of increased water usage and to permit adequate handwashing.

The largest outbreak of shigellosis reported in 1956, involving 800 cases, resulted from contamination of a public water supply by a mountain stream polluted with fecal waste. Three of the outbreaks resulted from the *sonnei* type of organism, and three from the *flexneri* type. *Shigella alkalescens* was isolated from specimens collected during one of the outbreaks, and in another, no specific organism was found.

Staphylococcal Food Poisoning

In 1956, there were 111 outbreaks of staphylococcal food poisoning with 4,313 cases reported as compared with 102 outbreaks with

Table 1. Foodborne and waterborne disease outbreaks reported in 1956 by vehicle of infection

Area	Water		Milk and milk products[1]		Other foods[1]	
	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases
United States	9	1,719	31	873	210	11,133
New England:						
Maine	---	---	---	---	11	227
Vermont	---	---	---	---	2	98
Massachusetts	---	---	---	---	8	129
Rhode Island	---	---	---	---	1	24
Connecticut	---	---	---	---	4	162
Middle Atlantic:						
New York	1	6	1	68	9	593
New Jersey	---	---	---	---	4	167
Pennsylvania	---	---	---	---	2	38
East North Central:						
Ohio	1	700	---	---	7	38
Indiana	---	---	---	---	5	324
Illinois	---	---	1	9	10	528
Michigan	---	---	---	---	3	269
Wisconsin	---	---	---	---	1	11
West North Central:						
Minnesota	---	---	---	---	3	102
Iowa	---	---	---	---	1	12
Missouri	---	---	1	13	4	238
North Dakota	---	---	---	---	2	72
Kansas	---	---	---	---	---	---
South Atlantic:						
Maryland	1	10	---	---	1	152
District of Columbia	---	---	---	---	2	39
Virginia	---	---	---	---	5	236
North Carolina	---	---	---	---	3	212
Georgia	---	---	---	---	3	383
Florida	---	---	---	---	7	182
East South Central:						
Kentucky	---	---	---	---	6	898
Alabama	---	---	---	---	1	60
West South Central:						
Arkansas	---	---	---	---	2	390
Louisiana	1	72	---	---	5	622
Texas	---	---	---	---	1	100
Mountain:						
Montana	---	---	---	---	1	700
Idaho	1	15	---	---	4	20
New Mexico	---	---	---	---	1	323
Utah	1	800	---	---	---	---
Nevada	---	---	---	---	1	25
Pacific:						
Washington	---	---	1	4	5	299
Oregon	---	---	---	---	6	52
California	3	116	1	80	73	3,331
Alaska	---	---	---	---	2	3
Hawaii	---	---	---	---	4	74
Puerto Rico	---	---	21	579	---	---
Virgin Islands	---	---	5	120	---	---
United States 1955	2	22	3	302	193	9,633
United States 1954	7	452	9	200	234	11,704

[1] Includes outbreaks among military personnel.

Table 2. Foodborne, waterborne, and other disease outbreaks by type of infection, reported in 1956

Area	Typhoid fever		Salmonellosis		Shigellosis		Trichinosis		Botulism		Staphylococcal food poisoning		Gastroenteritis		Toxic agents	
	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases
United States	7	52	23	1,999	8	1,107	11	98	11	22	[1] 111	[1] 4,313	[1] 88	[1] 6,688	[1] 9	[1] 160
New England:																
Maine	2	8	2	59			2	10			3	131	4	27		
Vermont	1	2									1	91	1	7		
Massachusetts											7	95	1	34		
Rhode Island													1	24		
Connecticut											1	20	3	142		
Middle Atlantic:																
New York	1	7	1	6					1	1	2	96	6	532		
New Jersey							3	34					1	133		
Pennsylvania							2	38								
East North Central:																
Ohio	1	6	1	9	1	12	1	2					5	718		
Indiana					1	11					1	7	3	306		
Illinois			3	131							7	206	1	200		
Michigan											2	229	1	40		
Wisconsin											1	11				
West North Central:																
Minnesota											2	56	1	46		
Iowa											1	12				
Missouri	1	27									2	220	3	31		
North Dakota			1	9							2	72				
Kansas															1	3
South Atlantic:																
Maryland													1	152	1	10
District of Columbia											1	19	1	20		
Virginia											4	192	1	44		
North Carolina			1	200			2	12								
Georgia			2	377							1	6				
Florida			1	6							3	146	3	34	1	2
East South Central:																
Kentucky									1	1	3	209	1	650	1	38
Alabama															1	60
West South Central:																
Arkansas											1	40	3	418		
Louisiana			1	38			1	2			1	6	3	648		
Texas			1	100												
Mountain:																
Montana											1	700				
Idaho									1	6	1	3	3	26		
New Mexico													1	323		
Utah					1	800										
Nevada													1	25		
Pacific:																
Washington			1	135							2	117	2	47		
Oregon					1	17					4	23	1	8	1	21
California	1	2	[illegible]	927	3	211			6	11	30	891	36	2,053	3	26
Alaska									2	3						
Hawaii			1	2	1	56					1	16				
Puerto Rico											21	579				
Virgin Islands											5	120				
United States 1955	5	36	16	971	10	475	5	92	5	14	102	4,130	66	5,160	5	99
United States 1954	16	92	26	1,164	19	1,471	6	53	8	18	100	4,868	103	5,914	10	279

[1] Includes outbreaks among military personnel.

4,130 cases in 1955. This represents a small increase in both number of outbreaks and number of cases over those for the previous year. During the past 3 years, the number of cases per year has exceeded 4,000. The 26 outbreaks with about 700 cases in Puerto Rico and the Virgin Islands might be considered as one single episode since all resulted from the same product, milk reconstituted from dry milk used in school lunch programs. Although only 36 outbreaks (33 *Staphylococcus aureus* and 3 *Staphylococcus albus*) were laboratory confirmed, there was enough epidemiological evidence to substantiate classification of the remaining outbreaks as staphylococcal food poisoning. In 1955, there were 15 laboratory-confirmed outbreaks and in 1954 the number was 26.

In about half of the outbreaks of staphylococcal food poisoning reported this year, lack of refrigeration or a food handler was given as the source of infection. A typical example of infection by a food handler is the outbreak reported in a high school, where 103 persons became ill following a turkey dinner. An investigation revealed that 1 of the 3 persons who deboned the turkeys had an infected burn on one finger. It was postulated that this individual infected about a third of the meat. The fact that about a third of those who ate turkey became ill from 2 to 6 hours later would seem to make this explanation a reasonable one.

Among the places most often mentioned in connection with these outbreaks of staphylococcal food poisoning were private residences and public eating places, with 18 outbreaks attributed to each. There were 15 outbreaks in schools and colleges, and in 12 outbreaks products from bakeries were considered to be vehicles of infection.

Gastroenteritis

Of the 88 outbreaks of gastroenteritis shown in table 2, 69 resulted from food other than milk and milk products. In these foodborne outbreaks, 5,100 persons were affected. In many instances, no food was available for laboratory tests, and in others, no pathogenic organisms could be isolated from the suspected food or from stool specimens from the patients. This is similar to the experience in previous years. Bacteriological tests on specimens from 4 outbreaks revealed paracolon organisms, and specimens from 3 yielded streptococci. In one outbreak, an unidentified gram-positive coccus was found.

Six outbreaks of gastroenteritis, with 903 cases, were waterborne, and 2 outbreaks, with 93 cases, were milkborne. In five outbreaks there was evidence of person-to-person spread, suggesting viral infections, but virus isolations were not made. An outbreak in Colorado was first thought to have been waterborne because routine examinations showed the water supply to be substandard, but investigation revealed that the cases were not related to water consumption. The outbreak was regarded as gastroenteritis of viral origin, a type of infection common in the area in certain seasons.

During the year, reports were received of 12 outbreaks of gastroenteritis (2,112 cases) in which turkeys were incriminated. Of these, 9 outbreaks were in schools, 2 in institutions, and 1 followed a church dinner. No etiological agent was found in any of these outbreaks. Some may have been due to salmonella infections, and others possibly were due to *Clostridium welchii*.

Trichinosis

Eleven outbreaks of trichinosis with 98 cases were reported in 1956. About the same number of cases were reported as for 1955, but the number of outbreaks more than doubled. In 1955, one outbreak with 69 cases was reported among members of two fraternities. In 1954, there was no large outbreak, but in 1953 one outbreak with 73 cases in an institution was reported. The largest outbreak in 1956, with 29 cases, resulted from sausage eaten in 3 counties of Pennsylvania. The source was a local butcher who supplied the pork product. In another outbreak, 12 cases developed in persons who ate a German delicacy supplied by a local butcher. One outbreak followed a cocktail party, and one was in a boys' camp. The remainder were in private families, including a

family gathering where only 2 persons developed the disease among the 14 present.

Botulism

Eleven outbreaks with 22 cases (9 deaths) of botulism were reported by 4 States and Alaska. In only one outbreak was the botulism organism isolated, this being type A. There was sufficient evidence, including clinical manifestations, to warrant a diagnosis of botulism in the other outbreaks. Most of the outbreaks involved only one case. However, in 1 outbreak, there were 6 cases (1 death) in a private family. These individuals had eaten home-canned beet greens. Four persons in another family became ill after eating string beans. In Alaska, there were 2 outbreaks, 1 from seal meat and 1 from whale meat, presumably type E infections. Although the organism was not recovered, a heat-labile toxin was found. Also, the investigator has recovered the same type of botulism organism previously in these kinds of meat. Other foods involved in the outbreaks were all home-canned products, including pickled pigs' feet, potatoes, and olives.

Toxic Agents

Two disease outbreaks were from arsenic poisoning, one from spray being blown from a peach orchard to a cabbage field. Sixty people who ate cabbage from this field became ill. The other episode of arsenic poisoning was in a rural family who drank water from a well which was deliberately contaminated with rat poison. Two outbreaks were attributed to food coloring—1 was caused by nitrite from the coloring used in weiners and 1 by copper found in a cake coloring. Three children became ill after playing with an insect spray. Soft drinks were the vehicles of infection from the remainder of the outbreaks. One outbreak resulted from the accidental contamination by insect spray of paper cups used for dispensing the soft drink. In another outbreak, cadmium from a container contaminated an acid drink. The other outbreak was copper poisoning which developed when a defective valve in a dispensing machine permitted carbonated water to back up and remain in contact with copper pipes. The ninth outbreak was due to antimony in an acid drink which had been left too long in a defective coffee pot.

Streptococcal Infections

Only 4 outbreaks of streptococcal food poisoning were reported; 2 were in school, 1 in personnel of the Armed Forces, and 1 in a private household. Three were associated with salads, two of them with egg salads. Although no organisms were isolated from the food, there was good evidence that food handlers had contaminated it. In 1955, egg salad was responsible for one large outbreak of streptococcal food infection reported during that year. A streptococcal organism was isolated from both the salad and the person who prepared it. One outbreak of two cases, in 1956, was from canned spaghetti and meat balls. It probably was contaminated in the home because unopened cans appeared to be normal.

Streptococcal infections not associated with food were reported from three schools and an Armed Forces training center. A total of 776 cases were reported in these 4 outbreaks.

Miscellaneous Outbreaks

During 1956, various outbreaks of illness not associated with food were reported. Some of the more important are summarized briefly in the following paragraphs.

Only two outbreaks of diarrhea of the newborn were reported in 1956. In one, *Escherichia coli* was found; in the other, alpha *coli* was reported as the etiological agent. Twenty-two infants were involved in these outbreaks. Another type of disease in newborn infants which apparently is increasing in frequency is characterized by staphylococcal skin infection. Six epidemics were reported among infants in hospital nurseries, and in some instances, the same serotype of organism was found in breast abscesses of some of the mothers who nursed these infants.

Another type of skin infection (erythema infectiosum) was reported among school children in four States and Hawaii. This infection was also found in some adults.

Several outbreaks of diphtheria were re-

ported, one of the largest being in Illinois. Here, 60 cases developed among migratory workers from Texas. Later in the year, during October, an outbreak occurred in a relatively low income group in which primary immunizations had not been given to most of the inhabitants. A total of 165 cases, with at least 2 deaths, were reported in Detroit in 1956. Smaller outbreaks occurred in Indiana and New Mexico. Other outbreaks reported in 1956 involved fewer than 10 cases.

Eight outbreaks of infectious hepatitis were reported in 1956. One outbreak with an undetermined number of cases was similar to one reported in 1955, that is, both were among members of a football squad who had been drinking contaminated water. Another 1956 outbreak of 276 cases was also considered to be waterborne and *E. coli* was isolated from water samples. Although water was associated with these outbreaks, there was no evidence which would definitely incriminate it. None of the outbreaks in 1956 were foodborne. In about half of the outbreaks there was evidence of person-to-person transmission, and for the other half, the source was not determined.

Localized outbreaks of arthropod-borne types of infectious encephalitis occurred in several parts of the United States in 1956. In Massachusetts, a group of 11 confirmed and 3 presumptive cases of the eastern equine type of infection was reported, and in Maryland, there were 3 human cases, 2 presumptive and 1 confirmed. This disease in horses and in pheasants was observed in these and several other States. Fourteen scattered human cases of western equine encephalitis in California and 16 in northwestern Texas were confirmed by serologic tests. A large urban epidemic, 110 cases with 13 deaths, of the St. Louis type of encephalitis was reported in Louisville, and another, consisting of 17 cases, in southwestern Kentucky. A sizable outbreak occurred in northwestern Texas, smaller ones in two areas of Colorado, and one in Kansas.

During the year, more than 500 cases of psittacosis in humans were reported. Most of these were single cases and resulted from contact with pet parakeets. However, outbreaks were reported in five States. Early in the year, the disease occurred in Oregon among a large number of persons who worked on turkey farms, in rendering plants which handled dead turkeys, and in employees of poultry processing plants. Two other small groups of cases were reported in which there was contact with infected birds. Ducks on a farm in Virginia were found to be infected with psittacosis, and at least four persons working on the farm became ill with the disease. In Minnesota, seven persons who became ill with psittacosis had contact with Easter chicks. No virus was found in any of the chicks.

Only one outbreak of brucellosis was reported, this being milkborne. It involved four children who drank raw milk. There were several single cases of the disease from raw milk. Others were from handling cow or hog carcasses in processing plants. In Maine, Newcastle disease was reported among poultry flocks, and one human case is known to have occurred.

Tomorrow's Challenges To the Medical Sciences

AN audience of about 100, composed predominantly of officials of major American corporations, heard the Honorable James B. Conant, retiring Ambassador to West Germany, introduce and summarize three panel discussions on the prospective need for medical research and teaching at a conference on Tomorrow's Challenges to the Medical Sciences, held at the University of Chicago, March 5, 1957. The meeting was sponsored by the National Fund for Medical Education in cooperation with the International Harvester Foundation and the United States Steel Foundation.

Dr. Conant, former president of Harvard, distinguished chemist, and author of On Understanding Science, flatly supported the case for corporate contributions to medical schools, saying, "This money will go to protect the health of your employees and customers. Your stockholders will get their money back." This comment was offered in response to the question raised by one corporation official who said he doubted that he could justify use of stockholders' funds to endow teaching hospitals or medical schools.

A sum between $500 million and $1 billion over the next 20 years was estimated by Dr. Vernon W. Lippard of Yale University School of Medicine as needed to meet increased operating and maintenance costs in private or independent medical schools. He said 25 new medical schools will be needed by 1975 (7 are in prospect, 4 of them expansions of 2-year schools) and that the number of graduates per year should be 200 more than at present. However great the cost, he observed, Americans spend more money each year on tombstones than on medical education.

Apart from these quantitative changes, indicated by the increase in population, growing industrialization, and urbanization, with the concurrent increase in demand for health services, the panels discussed impending changes in the character of medical knowledge and applications.

Dr. Stafford L. Warren, University of California School of Medicine, Dr. Austin M. Brues, University of Chicago College of Medicine, and Dr. A. Baird Hastings, Harvard Medical School, commented on the implications to medicine of nuclear physics: the new knowledge of biochemistry revealed by radionuclides used to trace chemical processes; the need to evaluate genetic and somatic hazards of radiation exposure and to develop protective measures; the probable environmental effects of nuclear power plants; the application of electron micrography to analysis of macromolecules and viruses; and the employment of radiations in diagnosis and therapy.

Dr. Brues expressed confidence that evaluation of the hazards of radiation, both internal and external, would progress rapidly enough to permit effective protective measures to be applied.

Recent changes in knowledge were said to require wholesale revision of textbooks and study courses. And the increasing range of scientific information of concern to the physician, it was suggested facetiously, might add up to a 16-year study course. But the panel was confident that selectivity, both with respect to learning and the learners, would permit physicians to begin practice long before they are old enough for retirement.

Many changes in physiological concepts were attributed to studies with radionuclides, which Hastings likened to birdbanding. For example, radionuclide studies showed that cells exchange salts, contrary to the indications of chemical studies. The rate of such exchange is a phase of metabolism. Hastings also mentioned a 3-year study which succeeded in changing "or" to "and." Demonstrating that diabetes consists of overproduction and (not or) underconsumption of sugar, the study resolved a longstanding controversy.

Hastings concluded that biological education for medical students today is less than what any educated man should receive in order to live intelligently in today's world. He felt a balanced education would give 60 percent of the time to humanities and social studies and 40 percent to the medical sciences.

Another radionuclide discovery, that animals

consume carbon dioxide, forced revision of the precept that life is like a burning candle: It is not.

The importance of selecting and motivating medical students effectively, in light of increasing responsibilities of the physician, anticipated the discussion of the behavioral sciences by a panel including Dr. Donald G. Marquis, University of Michigan, Dr. John Romano, University of Rochester School of Medicine, John M. Stalnaker, president of the National Merit Scholarship Foundation, and Theodore O. Yntema, vice president in charge of finance, Ford Motor Co.

Marquis noted that the behavioral sciences concern all professions in that they attempt to apply scientific method to the social studies. Much of his discussion was devoted to describing the scope and potentialities of the behavioral sciences.

Stalnaker indicated how behavioral sciences may be applied specifically to the difficult and complex task of selecting candidates for medical education with particular concern for that half of the top quarter of high school graduates who do not go on to college.

Romano's remarks dealt with the challenge of mental health, as an aspect of the behavioral sciences, and he discussed modern psychiatric methods with respect to their similarities to and differences from other scientific studies. Despite the handicap of psychiatric studies, that subjects are not as amenable to control or manipulation as the material of the physics laboratory, the body of common experience and observation was found to be testing and refining psychiatric theory. Major objects of interest to the psychiatrist continue to be the study of brain-mind phenomena, brain-mind-body relationships, and the field of interpersonal relationships. In particular, Romano commented on the significance of separation from and loss of key human figures in one's life as determinants of mental and physical disabilities.

To accommodate the need for extending medical learning in radiology, behavioral sciences, and other new developments, Yntema recommended extending the process of selection and preparation for advanced education into the early years of childhood. He felt far better use could be made of time spent in elementary and secondary schools, not to mention medical schools. Since scientific progress often means simplification of concepts, he suggested that many advances may in fact short-cut traditional courses of instruction. Educational processes, he indicated, might be rationalized as successfully as automobile production processes.

Following other comments, questions, and discussions, Dr. Conant stressed the opportunity industry has of extending scientific knowledge for the benefit of civilization, the administrative skills which industry may contribute to scientific investigation, and the opportunity for using industrial plants as a channel for popular health education and for improvement of medical care and public health practice. For leadership of such developments, however, he said, look to the faculties and graduates of medical schools.

Grants for Advanced Nurse Training

The Public Health Service has granted 587 awards for advanced nurse training in teaching, supervision, and administration; 553 of the awards are for full-year courses and 34 for spring or summer sessions. The Service has completed allocation of $2 million appropriated by Congress August 1956 for the first year of the 3-year program.

Half of this year's trainees in 56 schools of nursing and public health are preparing for teaching positions. Of the other half, 28 percent are training for administrative posts and the remaining 22 percent, for supervisory positions.

PERFORMANCE ON A CANCER KNOWLEDGE TEST BY Medical and Osteopathic STUDENTS

DAVID A. WOOD, M.D., PETER G. LORET, Ph.D., and LEONARD W. TOWNER, Ph.D.

ANNUALLY since 1949, the majority of the medical students in the United States have taken the Examination for Students of Medicine in the Subject Matter of Cancer, developed and administered by the education project of the Cancer Research Institute at the University of California School of Medicine. In 1952, two osteopathic colleges entered the testing program, and since 1953, all the osteopathic colleges in the Nation have participated. The same test has been administered to both medical and osteopathic students each year, although the test itself has undergone annual revisions.

The examination attempts to evaluate students' knowledge of cancer. It consists of 150 multiple-choice items in which the subject is asked to select the best of 5 alternative responses. The major aspects of the examination have been discussed in previous publications (*1–5*). Briefly, it covers a representative sampling of all types and locations of tumors and deals with three major aspects of these neoplasms: diagnosis, characteristics, and treatment.

Dr. Wood is professor of pathology and director of the Cancer Research Institute, University of California School of Medicine. President of the American College of Pathologists from 1952 through 1955, he is now president of the American Cancer Society. Dr. Loret is assistant research oncologist (medical education) with the Cancer Research Institute, and Dr. Towner, now assistant professor of psychology, Long Beach State College, Long Beach, Calif., was formerly with the institute.

The education project of the Cancer Research Institute, which conducted the study reported here, is supported by a grant from the National Cancer Institute, Public Health Service.

In this paper, we shall consider the relative performance of medical and osteopathic students on this test. All valid tests available from the medical and osteopathic schools for 1953, 1954, and 1955 were studied to determine (*a*) distributions of individual scores, (*b*) distributions of school means, and (*c*) mean percentages of correct responses in the areas of diagnosis, characteristics, and treatment of neoplasms. In addition, test results for the medical students for 1949–55 and for the osteopathic students for 1953–55 were analyzed for an estimate of the increases in mean raw score since the first year of participation in the testing program.

The number of students whose tests were included each year from 1953 through 1955, the major period of the study, are given in the accompanying table.

Individual Scores and School Means

The distribution of the individual raw scores for each medical class and for each osteopathic class each year of the study (freshmen, sophomores, juniors, and seniors, 1953–55) was plotted in frequency polygon form. These distributions are all similar in configuration. In each of the 3 years, the mean score for osteopathic freshmen exceeded the mean score for medical freshmen.

When the means of these distributions are plotted in histogram form, as shown in figure 1, several additional trends are revealed. The data indicate not only that the mean score for the osteopathic freshmen was above the mean score for medical freshmen every year, but also that the magnitude of this difference has increased with each succeeding year. This may be attributable partly to the fact that the osteopathic schools devote considerably more time to cancer teaching in the freshman year than is customarily the practice in medical schools.

Another notable trend shown in the data in figure 1 is that the differences between the osteopathic and the medical mean scores for the sophomores, juniors, and seniors have gradually decreased since 1953.

Statistical determination of the significance of differences in mean scores between the 4 medical and the 4 osteopathic classes for each of the 3 years was accomplished by means of the critical ratio. In 11 of the 12 comparisons the difference between the mean score of the medical students and the mean score of the osteopathic students was significant well beyond the 1 percent level of confidence. This level of confidence implies that there is less than 1 possibility in 100 that the observed difference is due to chance. In the 12th comparison, that of the 1955 sophomore classes, the difference was significant at the 5 percent level of confidence.

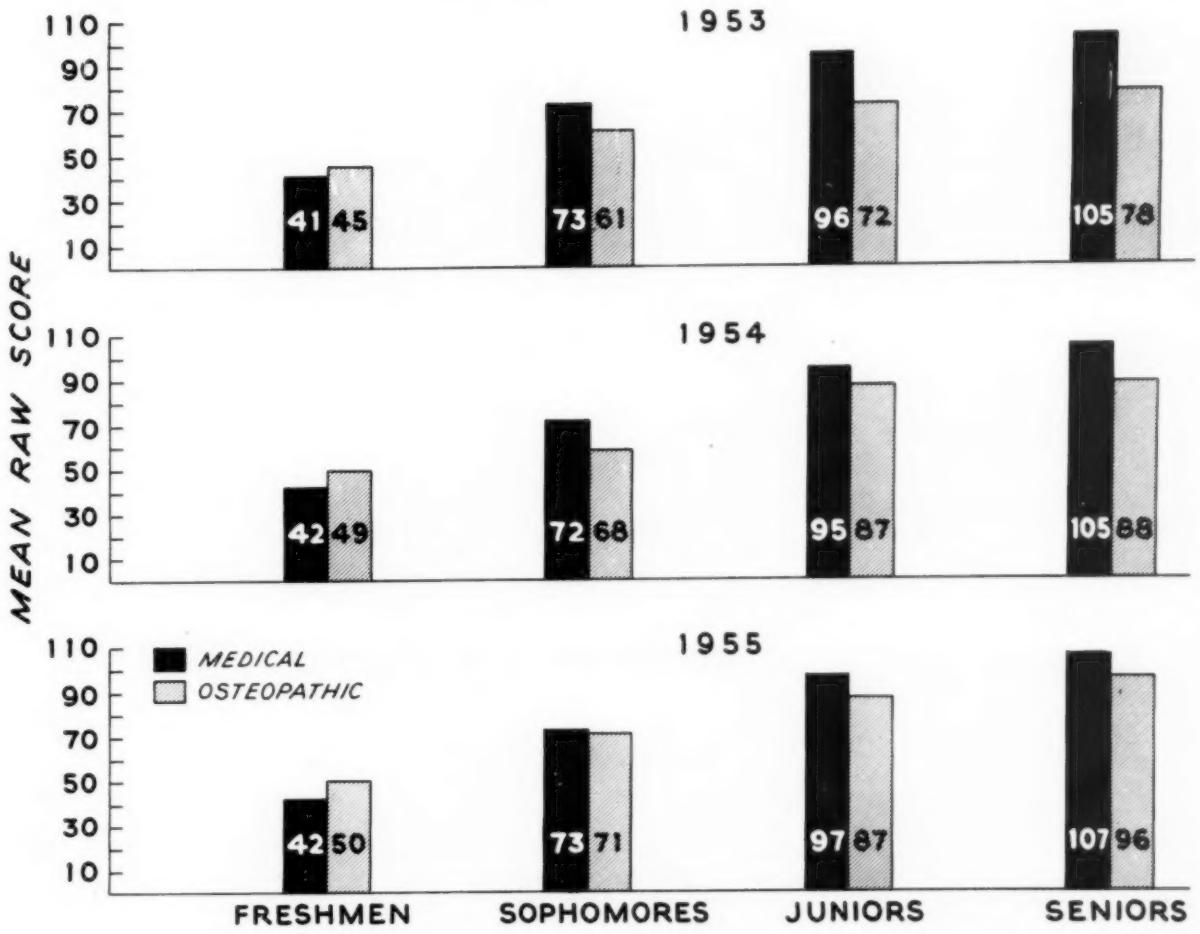
Statistical significance, of course, does not necessarily imply a meaningful difference when the number of individuals involved is very large, as is the case here. It is a matter of judgment as to how many points' difference constitutes educational significance in terms of the students' actual knowledge of the subject matter of cancer. Nevertheless, the educational effort required to overcome this difference with such a large number of students could itself be considered significant.

The distributions of school means for each class each year show trends similar to those of the individual raw scores. The mean scores of the osteopathic schools at the freshman level tend to fall above the mean scores of the medical schools, and the distributions of school means for the upper three classes are similar in shape

Number of medical and osteopathic students taking the cancer knowledge examination, by year

Year	Medical students				Osteopathic students			
	Freshmen	Sophomores	Juniors	Seniors	Freshmen	Sophomores	Juniors	Seniors
1953	4, 713	4, 808	4, 287	3, 727	492	458	447	380
1954	4, 174	4, 191	3, 957	3, 166	363	380	361	294
1955	4, 324	4, 295	3, 904	3, 369	361	345	364	324

Figure 1. Mean raw scores for medical and osteopathic students on the cancer knowledge examination, 1953–1955.



to those of the raw scores. In each of the last three cases, the mean of the medical school means falls above that of the osteopathic school means.

Scores in Specific Areas

The average percentage of correct responses obtained in 1955 by the medical and osteopathic students on items dealing with the diagnosis, characteristics, and treatment of tumors is shown in figure 2. The osteopathic freshmen consistently scored higher than the medical freshmen in each of the three areas, while, with one minor exception (the sophomores in the area of treatment), the osteopathic sophomores, juniors, and seniors scored slightly below the corresponding medical students. Available longitudinal data show increases in percentage between 1953 and 1955 for all of the areas at all four class levels for both types of schools, although these increases have been somewhat more marked in the osteopathic schools. One might expect to find particularly great differences in the area of treatment, but figure 2 shows that this is not the case. Apparently, the patterns of cancer knowledge of medical and osteopathic students are quite similar.

Comparisons of Initial Gains

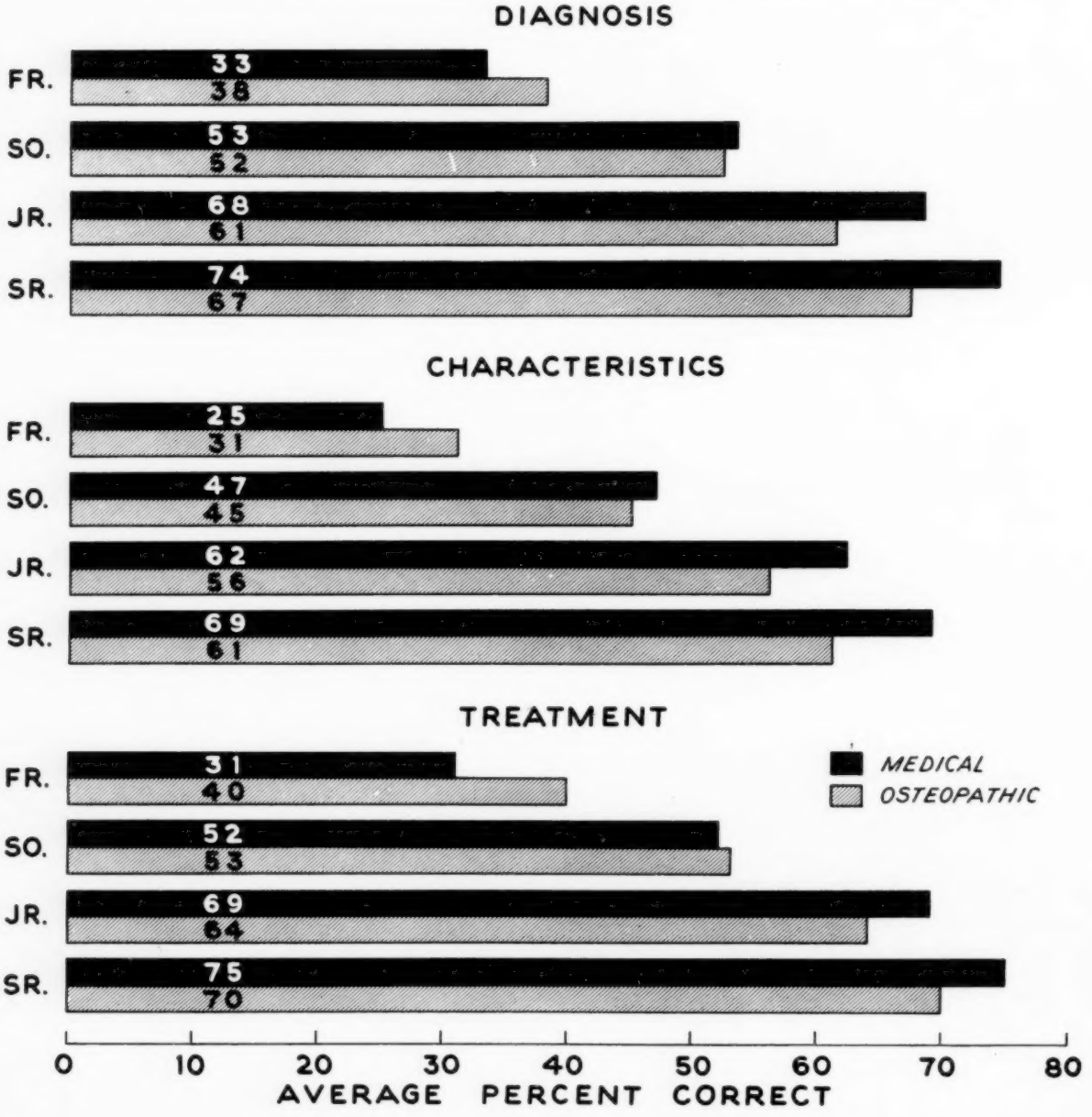
The increases in mean raw score since the initial year of participation are of particular interest as measures of the development of the cancer teaching programs in the two types of schools under consideration.

Since 1949, the initial year of participation by medical schools, there has been a steady increase

in the mean scores of the sophomores, juniors, and seniors, while the mean freshmen scores have tended to remain at a constant level. This latter phenomenon is to be expected since there is little reason to believe that freshmen in the medical schools in 1955 knew any more about cancer than did the freshmen in 1949. However, corollary data collected by the education project suggest that there has been a steady improvement in the content and method of cancer instruction for the upper classes in medical schools.

The teaching of cancer in the osteopathic schools shows similar trends. Since 1953, the osteopathic students' initial year of participation, these students have shown a relatively greater degree of gain than did the medical students during their first 3 years of participation. Both types of schools, however, show evidence of improvement in cancer learning.

Figure 2. Mean percent correct scores for medical and osteopathic students in the areas of diagnosis, characteristics, and treatment on the cancer knowledge examination, 1955.



Summary

From a study of the relative performance of medical and osteopathic students on a test of cancer knowledge, the following major findings are evident:

1. The mean raw score for freshmen students of osteopathic schools exceeded that of freshmen of medical schools for all 3 years, 1953, 1954, and 1955.

2. The mean raw scores of sophomore, junior, and senior students in medical schools exceeded those of the osteopathic students for all 3 years. The magnitude of the difference between the respective classes for the two types of schools, however, has decreased from year to year.

3. In each of the three areas—diagnosis, characteristics, and treatment—the osteopathic freshmen students consistently obtained higher scores than the medical freshmen. At the sophomore, junior, and senior levels, however, the mean percent correct for the medical students exceeded that for the osteopathic students, with one minor exception.

4. All classes in both types of schools have shown increases in the mean score for the areas of diagnosis, characteristics, and treatment of cancer. These increases have been somewhat more marked in the osteopathic schools.

5. Since their initial participation in the cancer testing program, both types of students have shown improvement in cancer learning. The degree of improvement has been somewhat more rapid for the osteopathic students, although their performance during the sophomore, junior, and senior years is still below the performance level of medical students.

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Mental Health Services in Colorado Schools

A 3-day workshop was held recently in Denver on mental health services in Colorado schools. A joint project of the Colorado State Department of Public Health and the State Department of Education, the workshop was supported by a grant from the National Institute of Mental Health, Public Health Service.

Represented at the conference were workers in clinical psychology, psychiatry, social work, school psychology, school administration, public health, and school and public health nursing. Participants came primarily from outlying districts of the State, where there are few mental health services in schools.

The conference defined the roles of professional mental health workers so that their services may be better used by educators to meet everyday school problems. Ideas were developed on the planning of mental health services at the local level, already reflected in concrete planning by some Colorado communities.

Training New Sanitarians in Virginia

CONLEY W. WESTON, B.S.

EVERY community in Virginia today is served by an organized health department. Ten years ago such services were available to only one-half the State. Concomitant with this rapid growth in local health units has been the demand for broader services to match a higher standard of living and changes in the social structure.

The expansion of both health units and programs imposed upon the public health administrative force of the State the problem of recruiting personnel to fill the new positions and to provide the varied services anticipated by the public.

Especially difficult was the recruitment of enough sanitarians to staff the new jobs. Furthermore, turnover in this field often exceeded replacements, and many positions remained vacant for extended periods. The inadequacy of the staff and recruiting program of the Virginia Department of Health in coping with the situation prompted the search for a solution.

Early in 1952 the Virginia Department of Health launched a study of its recruiting and training needs. Training programs and salary scales for sanitarians in other States were reviewed, and the resources of industry, universities, and the Public Health Service were used. The State then designed a recruiting and training program that was geared to its own requirements.

Two major characteristics of the program are, first, flexibility to facilitate modifications and, second, tying in training with recruiting. Fused with this process is the understanding of the need for frequent salary changes.

The administrative responsibility for the inservice training program is assigned to the Virginia Department of Health. A section of sanitation training was established in the division of local health services to plan, coordinate, and evaluate the training. Program costs are borne by the State health department, with county health departments paying a percentage of trainee salaries. Recruiting is centralized at the personnel bureau of the State health department.

The basic structure of the program involves the following major stages:

- Recruiting and indoctrinating new sanitarians.
- Supervising new sanitarians while on the job.
- Giving new sanitarians 12 weeks of basic fundamentals in sanitation.
- Conducting topical short refresher courses for experienced sanitarians.
- Offering academic study leading to the master of public health degree for qualified, experienced sanitarians.

Recruiting and Indoctrination

A job description, offering an attractive salary range, limits recruits to college graduates preferably with a major in the physical or biological sciences. Throughout indoctrination, recruits are screened by tests, interviews, and followup of references in order to weed out those unsuited. The personnel bureau carefully explains the entire inservice program to the applicant, who, on his acceptance of the

Mr. Weston is director of the sanitarian training section of the Virginia Department of Health. *The paper was read in essentially the same form at the Conference of State Directors of Public Health Training in Atlantic City on November 11, 1956.*

position, enters a 6-month probationary period. He receives full salary and living expenses during indoctrination and away-from-home assignments. The trainee's services are subject to immediate termination either voluntarily or by his employer.

On his first day of employment, the recruit is sent to 1 of 4 indoctrination centers located in county health departments, staffed with local workers and jointly operated by the State and county health departments. The four departments were selected to serve as official indoctrination centers because they are staffed by trained personnel engaged in broad, working sanitation programs. One sanitarian in each official center is appointed trainer, and his salary is increased for this service.

During indoctrination the recruit is observed closely as he follows a supervised course designed to fit his individual abilities. In this course he is introduced to the overall public health field. Public health philosophy, principles, programs, practices, and organization and administration are gradually unfolded for him. He observes community organizations, and government and nonofficial agencies and their impact on public health practices. Besides learning the value of teamwork in public health, he can develop his skills and techniques through supervised observation and practice in some sanitarian activities.

At the same time, the trainer studies and evaluates his progress and potential, keeping careful records and making periodic reports. The recruit may stay at the center from 4 to 6 weeks, depending on his progress, after which he enters the next phase of training in the field. Many recruits do not measure up to expectations during indoctrination and are therefore eliminated at this point; 20 percent of recruits in 1956 proved unsuited for further study in the program.

Supervision While on the Job

The new employee is next assigned to a job in the field where he is closely guided by his health director and supervisors until he demonstrates his ability to work with minimum help. This is his proving period in which he must show enough growth, potential, and performance to warrant ending the probationary period of employment. At this stage his tenure is usually from 4 to 12 months.

Twelve Weeks' Sanitation Course

Finally, the trainee is given a course in basic sanitation offered in a centrally located field training station in one of the local health departments. This course, limited to 16 students in a session, is planned for the inexperienced sanitarian with 4 to 12 months of field practice in sanitation. The trainee lives with others in his group in a nearby hotel throughout the 12 weeks. This stage of training may prove the most profitable because he continues his study of sanitation in off-duty hours through group discussions with other trainees and through project assignments.

One director and an assistant staff the field training station, for which teaching personnel are drawn from State and local health departments, private industry, and nearby colleges.

Basic fundamentals in the component parts of sanitation are taught along with functional program operation. Methods of teaching follow a pattern of classroom lectures, conferences, planned field observation, then practice under supervision. Trainees are graded on performance and accomplishment. To measure trainee growth and to improve instruction, the testing criteria of the American Public Health Association are used in addition to other materials. Those who graduate from the 12 weeks' course become full-fledged sanitarians, capable of handling their assignments with a minimum of direction. Thus far 124 candidates have successfully completed the course. But training opportunities have not stopped.

Refresher and Advanced Training

To maintain organization esprit and keep the experienced sanitarian stimulated and abreast of developments in sanitation, short refresher courses are held in selected components of the subject every year. Lasting from 2 to 10 days, the courses are offered at locations within commuting distance and are limited to 30 participants for each class. Usually the teaching

staff is drawn from the same sources as for the 12-week basic training course.

Topical refresher, short courses have been held in such sanitation components as water supplies and sewage disposal, insect and rodent control, sanitary milk control, food service, swimming pools, and advanced practices in supervision. More than 100 experienced sanitarians, including supervisory staff, have attended some or all of these refresher courses.

The final stage of training is professional study in a recognized school of public health leading to a master of public health degree. Provisions have been made for a limited number of qualified sanitarians to pursue this study.

Training Accomplishments

We have not as yet discovered or developed sufficiently accurate criteria for evaluating results of the program, but certain available data indicate general trends.

Job turnover in sanitarian personnel has decreased markedly since the program's inception. The department lost 7 percent by resignation of sanitarians in 1952 against 32.7 percent in 1951. The loss remained constant at about 10 percent during 1953–54. Late in 1955 resignations increased, and job turnover climbed to 18 percent. This was immediately met in 1956 with small salary increases.

The morale of the sanitarians is higher: They appear to be more satisfied and secure in their positions, want the training, and avail themselves of every opportunity to attend courses. It is no longer necessary to encourage or compel their attendance.

Health directors reflect their approval of the program by cooperating fully in its support. At first they preferred utilizing the services of the new employee to sparing him for training. Now however they demand that the sanitarian be trained. Finally, complaints from the public concerning sanitation services have decreased.

Although we hesitate to state that our training program is complete, we are convinced that certain segments of it are essential to meet the needs of our health projects within the State.

Concentration of Carbon Tetrachloride

A standard prescribing the maximum acceptable concentration of carbon tetrachloride in the atmosphere of working places was approved and published by the American Standards Association in June 1957.

The Public Health Service acted as endorsing sponsor for the standard and recommended its approval. Public Health Service participants in the development of the standard were Dr. W. F. von Oettingen of the National Institutes of Health, who served as chairman of the subcommittee engaged in the preliminary work, and Dr. H. E. Stokinger of the Bureau of State Services.

This standard is one of a series prepared by Committee Z37 of the American Standards Association. The committee coordinates information on air contaminants and establishes acceptable allowable concentrations, which are of use in developing methods for controlling such contamination.

Copies of the carbon tetrachloride standard, known as American Standard Maximum Acceptable Concentration of Carbon Tetrachloride, may be obtained for 50 cents from the American Standards Association, Inc., 70 East 45th Street, New York 17, N. Y.

Rheumatic Fever Prevention in Utah

L. GEORGE VEASY, M.D.

THE RHEUMATIC FEVER prevention program of the Utah State Department of Health is an outgrowth of a pilot program initiated by the Children's Bureau in an attempt to reduce the State's excessively high death rate from this disease. For the 3-year period 1939–41 the crude death rate from rheumatic fever in Utah was 22.4 per 100,000, higher than the rate for any other State and approximately double the national average (*1*).

The pilot program, begun in 1940 and continued through 1952, provided diagnostic and treatment services in clinics, hospital and convalescent care, public health nursing, services of a medical social worker, and nutrition consultation in Davis and Weber Counties only. In 1943 the program was extended to Box Elder, and later to Morgan, Summit, and Rich Counties. In 1952 the Utah State Department of Health assumed complete responsibility for the program and extended it to the entire State under its present direction. Unlike the pilot program, the present program does not offer complete care except in cases of total indigency. Principal emphasis of the program has been placed upon prophylaxis to conform to the overwhelming evidence that both the initial and recurrent attacks of rheumatic fever are precipitated by group A streptococcus infections.

During 1953–55, the first full 3 years of operation of the present program, 1,334 patients were seen. These patients were seen in itinerant clinics held in 10 centers of population scattered throughout the State. Each patient was referred to the program by his family physician, who requested one of the following referral categories for his patient:

1. Diagnostic consultation only.
2. Diagnostic consultation and followup to urge patient to continue prophylactic care in physician's office.
3. Diagnostic consultation with followup and prophylaxis in the Children's Heart Center.
4. Complete care (medical indigency only).

As of 1956, categories Nos. 3 and 4 were combined.

During the period 1953–55 more than 300 new patients were referred to the program each year (table 1). Approximately 50 percent of the 661 patients referred in 1953 were carried over from the program already in existence in the northern counties of the State.

In designing the program it had been hoped that most referring physicians would request that patients be placed in category 2. In so doing, it was felt that the public health nurse could assist the family physician in maintaining a closer followup of his patient while still under his management. However, the percentage of patients referred in this category has been disappointingly small, only about 25 percent.

A total of 209 patients in categories 3 and 4 have been followed for at least 6 months. The remaining 417 patients in these two categories

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Dr. Veasy is director of the children's rheumatic fever and heart program, and pediatric consultant, Utah State Department of Health. He is also clinical associate professor of pediatrics, University of Utah College of Medicine, Salt Lake City, Utah.

Dr. Joseph P. Kesler, acting director of the Utah State Department of Health, furnished guidance in establishing the present rheumatic fever program; Bessie Hansen assisted in the nursing program; and Ivy Jean Reid provided technical assistance.

This paper was presented in part at the First Scientific Convention of the Utah Heart Association, Salt Lake City, Utah, April 6, 1956.

have been divided into two groups, 120 cases of congenital heart disease and 297 cases which were closed because they failed to comply with the modified criteria of Dr. T. Duckett Jones (*2*). These 297 cases exceed by nearly 50 percent the number with a confirmed diagnosis and stress the great need for more accurate diagnosis of rheumatic fever.

We have adhered rigidly to the modified Jones criteria (*2*) and, to our knowledge, in only 3 of the more than 1,000 individuals referred to the program have we erred in not making the diagnosis of rheumatic fever. I am certain that this small number does not represent all the cases in which we have erred in diagnosis, but were the figure 10 times greater the criteria would still have been well over 90 percent accurate. To lend further support to the validity of the criteria of Jones, only four individuals with rheumatic heart disease had no history of an additional major manifestation of rheumatic fever.

Of the 209 patients followed for 6 months, 120 (60 percent) had only a history of rheumatic fever, with no residual heart disease. The 89 patients with rheumatic heart disease were categorically placed in the following functional and therapeutic classifications according to the standards of the American Heart Association: I,A, 55 patients; II,B, 30 patients; and III,C, 4 patients. No patients fell into functional classification IV or therapeutic classification D or E except temporarily, during an attack of acute rheumatic fever. Because classification IV,D was only temporary, these patients were included in a classification appropriate to their recovered status.

Table 1. Number of patients referred to the rheumatic fever program, Utah State Department of Health, according to referral category, 1953–55

Year	Category No.				Total
	1	2	3	4	
1953	162	151	317	31	661
1954	114	80	111	25	330
1955	123	78	123	19	343
Total	399	309	551	75	1, 334

If these patients represent an accurate cross section of the young people of Utah, the picture of the prevalence and severity of rheumatic heart disease is a far from dismal one. If the condition of these individuals can be stabilized at this point by the use of prophylaxis, the outlook is even more encouraging.

In evaluating the effectiveness of prophylaxis, we had only the histories of these patients before prophylaxis was started to compare with their condition after prophylaxis, since we had

American Heart Association Classification

Functional Capacity

CLASS I: Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

CLASS II: Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

CLASS III: Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

CLASS IV: Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency of the anginal syndrome are present even at rest. If any physical activity is undertaken discomfort is increased.

Therapeutic Classification

CLASS A: Patients with a cardiac disease whose ordinary physical activity need not be restricted.

CLASS B: Patients with cardiac disease whose ordinary physical activity need not be restricted, but who should be advised against severe competitive physical efforts.

CLASS C: Patients with cardiac disease whose ordinary physical activity should be moderately restricted, and whose more strenuous efforts should be discontinued.

CLASS D: Patients with cardiac disease whose ordinary physical activity should be markedly restricted.

CLASS E: Patients with cardiac disease who should be at complete rest, confined to bed or chair.

no control group with which to compare the study group.

Over 50 percent of the group had had only a single attack of rheumatic fever (table 2). Approximately a third had had two attacks, and less than 10 percent had had more than two attacks. No individual had had more than four recognized episodes of rheumatic fever. The average time between attacks, regardless of their number, varied from 2 to 2½ years. Generally speaking, the severity of the heart disease was proportionate to the number of attacks. However, 2 of the 4 patients in functional classification III had a history of only one episode of rheumatic fever.

Prophylaxis

The rheumatic fever prevention program has used four types of prophylaxis (table 3). There have been some recurrences of chorea, which will be discussed later. However, during the 3-year period of observation no individual who has maintained continuous prophylaxis has had an episode of clear-cut recurrence of acute "exudative" rheumatic fever with elevations of acute-phase reactants and antistreptolysin titers, with two possible exceptions.

The first patient, a 12-year-old boy, developed migratory arthritis of the knees and ankles, with redness and swelling, 2 months after starting on oral Bicillin. His erythrocytic sedimentation rate became elevated but his antistreptolysin O (ASO) titer showed no rise. He did not develop signs of carditis and he is still on Bicillin prophylaxis.

The second patient was a 13-year-old boy who was receiving oral penicillin prophylaxis. A routine electrocardiogram taken while following him for valvular heart disease with mitral and aortic insufficiency showed a right bundle branch block. He had been asymptomatic during the period in which the electrocardiographic abnormality developed. We had no ASO data on this patient.

Fifteen patients had classic murmurs of mitral insufficiency of class II or greater intensity on entering the clinic, which disappeared on followup examinations. Murmurs of aortic insufficiency disappeared in two persons while they were being followed. These patients are included in the group of 120 patients with only a history of rheumatic fever in categories 3 and 4. On followup examination, three individuals were moved from classification II,B to classification I,A. No patient with rheu-

Table 2. Number of attacks and average recurrence time among 209 rheumatic fever patients, Utah State Department of Health rheumatic fever program

Number of attacks	Number of patients	Average recurrence time (years)
1	126	
2	69	2.3
3	11	2.1
4	3	2.5

Table 3. Followup of prophylaxis of rheumatic fever patients, Utah State Department of Health rheumatic fever program

Type of prophylaxis	Daily dosage	Number of patients	Period of prophylaxis [1]	
			Total (years)	Average (years per patient)
Sulfadiazine	1.0 gm	27	54	2.0
Penicillin [2]	200,000 units	74	129	1.7
Bicillin [3]	200,000 units	113	130	1.1
Bicillin	1,200,000 [4] units	59	103	1.8
Total		273	416	1.5

[1] Continuous.
[2] Buffered penicillin G (Penioral, Wyeth).
[3] Benzathine penicillin (Wyeth).
[4] Per 30 days.

Table 4. Recurrences of rheumatic fever resulting from break in prophylaxis

Patient	Reason for break	Change in classification from—	Time between break and recurrence (years)
E. W	Sensitive to penicillin	History to I,A	1.2
B. P	Physician's advice	do	.2
B. T	Inadvertence in clinic	History to II,B	.3
R. L	Moved from State	History to I,A	1.0
S. N	Own volition	do	.2
D. L	do	do	1.3
L. P	do	do	.2
E. S	do	No change	.5

matic heart disease who maintained prophylaxis was reclassified in a lower functional classification during the 3-year period of observation.

Siblings of three rheumatic fever patients developed rheumatic fever while the patients were receiving prophylactic treatment. ASO titers were obtained from two patients before and during the time their siblings had rheumatic fever. No rise in titer was demonstrated.

Recurrence of Rheumatic Fever

Eight patients in categories 3 and 4 had recurrences of rheumatic fever (table 4). Each had had a clear-cut break in prophylaxis. Four patients discontinued prophylaxis of their own volition. In one, prophylaxis was inadvertently discontinued by me when I confused her with her sister. One patient moved from the State and had no followup until his return to our program a year later. Another had no prophylaxis because of a history of urticaria following ingestion of penicillin and exfoliative dermatitis following sulfonamide treatment. She since has been on oral Bicillin for 6 months without difficulty. One patient discontinued his prophylactic treatment upon the advice of his family physician.

The shortness of time between the discontinuance of prophylaxis and recurrence of rheumatic fever compared with the average recurrence time without prophylaxis has been striking. In some cases, the recurrence time has been so short that it is obvious that only year-round prophylaxis is completely effective.

Four patients who had broken prophylaxis developed significant (2 tube) rises in ASO titer. In no individual who maintained prophylaxis did we detect any significant rise in ASO titer.

Recurrence of Chorea

One of the most intriguing occurrences in the past 3 years has been the recurrence of chorea in nine patients who had maintained good prophylaxis. In none of these patients did "exudative" manifestations appear. There was no clinical, roentgenographic, or electrocardiographic evidence of progression of heart disease. Two patients required hospitalization. Chorea appeared in five patients between 3 and 4 months after it had been thought that all clinical evidence of rheumatic activity had disappeared. In three individuals, ASO determinations were done before, during, and after episodes of chorea. These titers showed a decline from the levels that had been present during their preceding acute episode of rheumatic activity. This lends rather strong support to the contention that chorea may be a greatly delayed manifestation of rheumatic fever. Two of the five patients who had early recurrence of chorea were on intramuscular Bicillin and three were on oral penicillin.

For the remaining four individuals, the time between the last clinically detected attack of rheumatic fever and the appearance of chorea varied from 2 to 4 years. Three patients were on oral penicillin. Their chorea appeared in 1953, at a time when we did not have an accurate record of the penicillin dispensed in the clinic, and we have only the word of the parents

and the patient that prophylaxis was maintained. The fourth patient was on oral Bicillin and, according to our records and her own statements, she had received continuous prophylaxis. She showed no rise in ASO titer with the appearance of her chorea.

Fourteen patients with acute rheumatic fever received "large dose" hormonal therapy as recommended by Kelley and his group (*3*). All 14 had clear-cut clinical evidence of valvular heart disease at the onset of the institution of hormone therapy. Nine showed complete regression of heart damage so that there is no detectable residual at the present time. Five showed a persistence without progression of the heart damage. In no individual was there any detected progression of the severity of the already existent heart damage.

Four patients in the group had received penicillin for their preceding streptococcal infections, but had gone on to develop rheumatic fever. The dosages could not be determined, but in no case was penicillin continued for more than 3 days.

The small number of adverse reactions to prophylaxis has been encouraging. Sulfadiazine was discontinued on two patients because of a morbilliform rash, which disappeared upon withdrawal of the drug. Had we been able to follow these two individuals more closely, prophylaxis probably would have been resumed. Oral penicillin was stopped in 3 patients who developed urticaria and in 2 who developed a morbilliform rash. All five reactions reappeared upon readministration of the drug.

We have observed no reactions to oral Bicillin and have recorded no cases of gastric intolerance to this drug. Three patients developed urticaria while on intramuscular Bicillin. Bicillin was discontinued in 11 other cases because of local intolerance and extreme emotional reaction to injection of the drug. Tolerance to Bicillin injection has varied greatly; some patients have been greatly upset and others have not been bothered at all. Because we have had to discontinue Bicillin in 25 percent of our patients, we do not feel that it is satisfactory for routine clinic use. We are certain, however, that it is effective and that, if used wisely in individual patients, it could well prove to be one of the more valuable forms of prophylaxis.

Followup

The most disappointing phase of our program has been the handling of patients in category No. 2 (those who had been seen in the clinic for a diagnostic visit and later followed by the family physician and the local public health nurse). We do not know the exact status of these individuals at this time. Reports from the local public health nurses are discouraging. Maintenance of prophylaxis has been poor, and unconfirmed recurrences of rheumatic fever have been reported. What had been hoped would be the most successful phase of our program has thus far proved to be the most inadequate.

According to reports of the local public health nurse, only 62 (50 percent) of the 122 patients in category No. 2 have maintained prophylaxis. The remaining 60 gave the following reasons for discontinuing prophylaxis:

Advice of family physician	22
No reason given	18
Too expensive	17
Language barrier	1
Urticaria (oral penicillin)	1
Advice of chiropractor	1

These figures support the author's opinion that the key to maintaining prophylaxis is the active participation of the family physician. One-third of the patients who discontinued prophylaxis did so on the advice of the family physician. Another third stopped because of a lack of awareness or of regard for the value of prophylaxis. Apathy of patients toward prophylaxis, I feel, can be overcome by the family physician who is sufficiently enthusiastic and convincing.

Assistance from public agencies or modification of the type of prophylaxis could solve the very real problem of expense for many families. Increasing the amount of penicillin should not be recommended until it is conclusively shown that it will result in an appreciable decrease in the recurrence rate of rheumatic fever, since the additional expense would

be likely to result in complete discontinuation of prophylaxis.

Physician Education

It was hoped that the program would serve as a good medium for educating the referring family physician regarding criteria for the diagnosis of rheumatic fever and the value of prophylaxis. To determine how well this purpose has been served, the percentage of agreement between the referring physician's diagnosis and the clinic diagnosis and the percentage of rheumatic fever patients who were on prophylaxis when they were referred to the clinic were determined for each of the 3 years. In 1953, allowing a very liberal interpretation, the referring diagnosis agreed with the clinic diagnosis in 56 percent of the cases. In 1954 there was no appreciable difference (59 percent), but in 1955 this percentage had risen to 70 percent.

In 1953 only 4 percent of the individuals with rheumatic fever histories referred to the clinic were receiving prophylaxis; in 1954, 12 percent; and in 1955, 31 percent. This last figure is low inasmuch as many referrals were made with the specific request for prophylaxis even though the patients had actually not been started on prophylaxis. We feel that we have definitely made some progress in the education of private physicians regarding the importance of prophylaxis for the prevention of rheumatic fever. We have been aided in this phase of the program by the educational campaign of the Utah Heart Association. However, physician education is still one of the weakest facets of our program.

Costs

The yearly costs of the program during 1953–55 and the yearly costs for 1948–50, a period when the program was confined to the six northern counties of the State, offered complete medical services, and maintained a small convalescent hospital, are compared below:

Former program		*Present program*	
1948	$22,590	1953	$17,168
1949	26,542	1954	10,017
1950	19,218	1955	15,704
Total	$68,350	Total	$42,889

The fact that the present program now serves 22 of the 29 counties of the State and includes patients with congenital heart disease as well as patients with rheumatic heart disease makes these figures even more impressive.

Conclusions

Although our experience with a program of rheumatic fever prevention during the past 3 years has not resulted in any new concepts, it has added strong support to certain previously accepted principles. Our findings and conclusions are as follows:

1. The modified Jones criteria are valid and offer the best available means for accurate diagnosis of rheumatic fever.
2. Continuous prophylaxis against group A streptococcal infections prevents recurrences of rheumatic fever.
3. The four types of prophylaxis evaluated—sulfadiazine, penicillin, buffered penicillin G and benzathine penicillin—appear to be equally effective.
4. To be completely effective, prophylaxis must be continuous.
5. In some individuals considered to be maintaining good prophylaxis, chorea appears as a "delayed" manifestation of rheumatic fever and occurs without evidence of a preceding streptococcal infection.
6. Active participation of the family physician is the key to providing continuous prophylaxis.
7. Rheumatic fever occurs when the initiating streptococcal infection is treated with inadequate doses of penicillin.
8. In patients with acute rheumatic fever, hormone therapy in sufficiently large doses, as recommended by Kelley (*3*), appears to be effective in stopping progression of heart damage.
9. To care for and control children with rheumatic fever and rheumatic heart disease, a program offering consultation and followup and primarily emphasizing prophylaxis is more effective and less expensive than a program offering complete care.

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Air Pollution and Radiological Courses

Pittsburgh. Various aspects of air pollution will be the subject of study in a new program leading to the degree of master of science in hygiene at the University of Pittsburgh Graduate School of Public Health, Pittsburgh, Pa. The program will begin in September 1957 and continue through August 1958. It is open to applicants who have an engineering degree and adequate training in chemistry. Preference will be given applicants with some years of experience in engineering.

The program has been organized to meet increasing governmental and industrial demands for air pollution engineers who are broadly educated and are able to deal with both the technical and administrative aspects of the air pollution problem.

A lecture and seminar course in air pollution will include study of health, nuisance, and agricultural aspects; causes, sources, and characteristic emission rates; meteorological influences; and rate of dispersion from a source. In an air pollution laboratory and seminar course, students will study and apply air pollution measurements. One half of the year will be devoted to measuring contaminants in community atmospheres and the other half to field exercises in measuring source emissions. From the end of the spring semester through August, the student will complete a research problem as part of the requirements for the degree.

In addition to instruction pertaining specifically to air pollution, the program's full curriculum is designed to provide students with a good understanding of the basic physical and social relationships between man and his environment. To this end, background courses such as principles of statistical reasoning, of epidemiology, and of public health practice; man and the environment; environmental physiology; industrial hygiene; industrial toxicology; and health physics are included.

Michigan. One of the country's first programs of integrated study in radiological health and safety will be offered by the University of Michigan School of Public Health, Ann Arbor, beginning in September 1957. The new program has been set up in response to growing demands for personnel highly trained in this field.

Courses scheduled to be given in September will be concerned with radioactive wastes and their disposal; the biological effects of radiation on man, plants, and animals; techniques used in studies of radioactivity; and methods of providing environmental protection.

The teaching and research staff in radiological health and safety has been expanded and the curriculum in environmental health reorganized to provide opportunities in the new program for intensive graduate study and for basic and applied research. In addition to teaching and research responsibilities, radiological health and safety staff members will assist in the university's program in the peacetime uses of atomic energy and will be represented in a team of University of Michigan consultants which has been requested to provide advisory services to the International Cooperation Administration.

publications

What Is Mental Illness?

PHS Publication No. 505 (Health Information Series No. 88). 1957. 2-fold leaflet. $3.00 per 100.

This leaflet describes briefly and generally the major classifications of mental disorders: the psychoses, the neuroses, and personality disorders. Also discussed are the causes of mental illness, what research is being done, facilities for treatment, and recovery chances for the mentally ill.

The importance of the attitude of the family and the community in rehabilitating the mentally ill is stressed.

Sunburn and Suntan

PHS Publication No. 104 (Health Information Series No. 1). Revised 1957. 1-fold leaflet. $2.00 per 100.

All persons interested in getting a suntan or in avoiding suntan and sunburn will find the information in this leaflet an invaluable aid. Discussed are exposure precautions, pharmaceutical preparations, and what to do in case of sunburn.

Salaries of State Public Health Workers, August 1956

PHS Publication No. 524. 1957. 41 pages.

The study of salaries paid to selected classifications of personnel employed by State and Territorial health departments is the eighth of a series started in 1947.

Data for this study were taken from August 1956 State and Territorial health department payrolls. It includes salaries of health officers; program directors of dental public health, sanitary engineering, laboratories, public health nursing, business administration, and directors of vital statistics or records (or both). Graphs and tables showing salary distributions are also included for the following occupational groups: medical personnel, exclusive of State health officers, sanitary engineers, sanitary personnel, public health nurses, nutritionists, health educators, analysts and statisticians, nonmedical administrators, dentists, veterinarians, and for the first time, medical and psychiatric social workers.

A major change in presentation of data is the tabulation by Bureau of the Census regions rather than by individual States. This change was made to expedite comparisons with other salary studies of national scope, which generally use the census regions to portray geographic variations.

Guide for a Tuberculosis Control Program for General Hospitals

PHS Publication No. 516. 1956. 12 pages. 15 cents

Discussed in detail are the essential elements of a tuberculosis control program for patients and personnel in general hospitals. Included are comprehensive plans for initial and followup examinations, and a time schedule for repeat tuberculin tests and chest X-rays.

A section is devoted to methods of coordinating hospital and other community services for the care of tuberculosis patients and their families.

Manual of Septic-Tank Practice

PHS Publication No. 526. 1957. 85 pages; illustrated. 35 cents.

The new Manual of Septic-Tank Practice has been prepared by the Division of Sanitary Engineering Services in cooperation with the Joint Committee on Rural Sanitation for use as a guide by health agencies, builders, installers, and others. It is the result of 5 years of study, laboratory research, and field trials. Much of the material is based upon results of extensive research carried on at the Robert A. Taft Sanitary Engineering Center, Public Health Service.

This work combines data from professional and technical organizations, official agencies, and industry. It also presents in one volume three previous technical reports on Studies on Household Sewage Disposal Systems.

Scientific Translations

A preliminary guide to sources and services

PHS Publication No. 514. 1957. 12 pages. 15 cents.

This guide represents an attempt to provide a directory of sources for finding and procuring translations of scientific literature, including data on cooperative translation programs, governmental agencies which collect or prepare translations, and a list of commercial translation services in the United States.

Although incomplete, the guide is offered at this time as a stopgap measure for meeting the critical need for information in this field.

This section carries announcements of all new Public Health Service publications and of selected new publications on health topics prepared by other Federal Government agencies.

Publications for which prices are quoted are for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. Orders should be accompanied by cash, check, or money order and should fully identify the publication. Public Health Service publications which do not carry price quotations, as well as single sample copies of those for which prices are shown, can be obtained without charge from the Public Inquiries Branch, Public Health Service, Washington 25, D. C.

The Public Health Service does not supply publications issued by other agencies.

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